L2 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:487749 CAPLUS
DOCUMENT NUMBER: 131:270182
TITLE: Hyaluronectin secretion by monocytes: downregulation by IL-4 and IL-13, upregulation by IL-10
AUTHOR(S): Girard, Nicole; Maingonnat, Catherine; Bertrand, Philippe; Vasse, Marc; Delpech, Bertrand
CORPORATE SOURCE: Groupe Merci, Universite de Rouen Centre Henri-Becquerel, Rouen, Fr.
SOURCE: Cytokine (1999), 11(8), 579-584
CODEN: CYTIE9; ISSN: 1043-4666
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hyaluronectin (HN) is a component of the extracellular matrix of connective tissue and is particularly associated with tumor inflammatory and connective stroma reaction, where it co-localizes with hyaluronic acid (HA). The HN/HA ratio has been suggested to be involved in tumor aggressivity and in the atherosclerosis process. IL-10 has also been described in atherosclerotic lesions and in cancer. HN production was therefore investigated in vitro in peripheral blood monocyte cell (PBMC) cultures, with and without bacterial lipopolysaccharide (LPS) or interleukins (ILs) in the medium. HN was characterized in monocytic cell cytoplasm and in culture supernatants. Anti-IL-10 antibody suppressed the LPS-stimulating effect on HN production HN synthesis rate was greatly increased in IL-10-activated cultures while IL-4 and IL-13, two other anti-inflammatory ILs, decreased HN release. In the presence of IL-10, the IL-4 or Il-13 inhibitory effect on HN synthesis was reversed. The results support the view that intratumoral release of IL-10 by monocytes may induce local production of HN. In conjunction with the known ability of HN to bind to HA, which is a cell migration and tumor invasion facilitating factor, and to inhibit HA-induced angiogenesis, our findings suggest that HN may modulate the effect of HA on atherosclerosis, angiogenesis and cancer development. (c) 1999 Academic Press.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:747947 CAPLUS
DOCUMENT NUMBER: 128:113555
TITLE: Hyaluronectin blocks the stimulatory effect of hyaluronan-derived fragments on endothelial cells during angiogenesis in vitro
AUTHOR(S): Trochon, Veronique; Mabilat-Pragnon, Christelle; Bertrand, Philippe; Legrand, Yves; Soria, Jeannette; Soria, Claudine; Delpech, Bertrand; Lu, He
CORPORATE SOURCE: 1 Ave Claude Vellefaux, Hopital Saint Louis, Bat. INSERM, Institut d'Hematologie, F-75475 Paris, Fr.
SOURCE: FEBS Letters (1997), 418(1,2), 6-10
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hyaluronic acid (HA) is a glycosaminoglycan of the extracellular matrix. Its fragmentation by the hyaluronidase, secreted by tumor cells, facilitates tumor invasion and the HA degradation products generated stimulate angiogenesis. The authors report here that the HA-binding protein hyaluronectin (HN) inhibits the stimulatory effect of HA-derived fragments on the proliferation and migration of endothelial cells in vitro, and hampers the organization of endothelial cells into capillary-like structures. Since HN strongly inhibits endothelial cell adhesion to immobilized

HA, it is postulated that HN acts by impairing the binding to endothelial cells of HA fragments generated by hyaluronidase, thereby neutralizing the effect of HA degradation products on angiogenesis. The authors' results reveal a new mechanism by which the angiogenesis induced by HA fragments is modulated by HN.

L2 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:450858 CAPLUS
DOCUMENT NUMBER: 125:139299
TITLE: Expression of hyaluronidase by tumor cells induces angiogenesis in vivo
AUTHOR(S): Liu, Dacai; Pearlman, Eric; Diaconu, Eugenia; Guo, Kun; Mori, Hiroshi; Haqqi, Tariq; Markowitz, Stanford; Willson, James; Sy, Man-Sun
CORPORATE SOURCE: Sch. Med., Case West. Res. Univ., Cleveland, OH, 44106, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1996), 93(15), 7832-7837
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hyaluronic acid is a proteoglycan present in the extracellular matrix and is important for the maintenance of tissue architecture. Depolymn. of hyaluronic acid may facilitate tumor invasion. In addition, oligosaccharides of hyaluronic acid have been reported to induce angiogenesis. We report here that a hyaluronidase similar to the one on human sperm is expressed by metastatic human melanoma, colon carcinoma, and glioblastoma cell lines and by tumor biopsies from patients with colorectal carcinomas, but not by tissues from normal colon. Moreover, angiogenesis is induced by hyaluronidase+ tumor cells but not hyaluronidase- tumor cells and can be blocked by an inhibitor of hyaluronidase. Tumor cells thus use hyaluronidase as one of the "mol. saboteurs" to depolymerize hyaluronic acid facilitate invasion. As a consequence, breakdown products of hyaluronic acid can further promote tumor establishment by inducing angiogenesis. Hyaluronidase on tumor cells may provide a target for anti-neoplastic drugs.

L2 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:694189 CAPLUS
DOCUMENT NUMBER: 123:101840
TITLE: Angiogenesis: Models and modulators
AUTHOR(S): Cockerill, Gillian W.; Gamble, Jennifer R.; Vadas, Mathew A.
CORPORATE SOURCE: Hanson Center Cancer Research, Institute Medical and Veterinary Research, Adelaide, 5000, Australia
SOURCE: International Review of Cytology (1995), 159, 113-60
CODEN: IRCYAJ; ISSN: 0074-7696
PUBLISHER: Academic
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with >250 refs. Angiogenesis in vivo is distinguished by four stages: subsequent to the transduction of signals to differentiate, stage 1 is defined as an altered proteolytic balance of the cell allowing it to digest through the surrounding matrix. These committed cells than proliferate (stage 2), and migrate (stage 3) to form aligned cords of cells. The final stage is the development of vessel patency (stage 4), generated by a coalescing of intracellular vacuoles. Subsequently, these structures anastamose and the initial flow of blood through the new vessel completes the process. We present and discuss how the available models most closely represent phases of in vivo

angiogenesis. The enhancement of angiogenesis by hyaluronic acid fragments, transforming growth factor β, tumor necrosis factor α, angiogenin, okadaic acid, fibroblast growth factor, interleukin 8, vascular endothelial growth factor, haptoglobin, and gangliosides, and the inhibition of the process by hyaluronic acid, estrogen metabolites, genestein, heparin, cyclosporin A, placental RNase inhibitor, steroids, collagen synthesis inhibitors, thrombospondin, fumagellin, and protamine are also discussed.

L2 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:612289 CAPLUS
DOCUMENT NUMBER: 103:212289
TITLE: Regulation of cell growth by vitreous humor
AUTHOR(S): Lutty, Gerald A.; Mello Robert J.; Chandler, Carol; Fait, Carolyn; Bennett, Alonzo; Patz, Arnall
CORPORATE SOURCE: Wilmer Eye Inst., Johns Hopkins Sch. Med., Baltimore, MD, 21205, USA
SOURCE: Journal of Cell Science (1985), 76, 53-65
CODEN: JNCSAI; ISSN: 0021-9533
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Exts. of normal vitreous inhibited angiogenesis in 2 animal models: tumor-induced neovascularization in the rabbit corneal micropocket and retinal extract-induced angiogenesis in the chick chorioallantoic membrane assay. Using in vitro assays, it was found recently that an extract of bovine vitreous, free of hyaluronic acid, inhibits proliferation of cells in the aortic wall, i.e., endothelium and smooth muscle cells, as well as capillary and corneal endothelium. The inhibition is dose-dependent, as determined by either cell amount or [3H]thymidine incorporation, and not due to cytotoxicity, as demonstrated with a double-label thymidine assay. The inhibitor is trypsin sensitive and heat stable (95° for 10 min). Conversely, proliferation of pericytes, lens epithelium, and fibroblasts (dermal and corneal) was stimulated by the vitreous extract This mitogenic activity was heat labile. Growth of pigment epithelium and several tumor cell lines was unaffected. Normal vitreous apparently contains a heat-stable growth inhibitor specific for endothelium and smooth muscle cells, and a nonspecific heat-labile mitogen. The paradoxical effect of this antiangiogenic factor on arterial and capillary contractile cells, smooth muscle, and pericytes, suggests a basic difference in the regulation of the 2 vasculatures. A substance in normal vitreous may be important in controlling neovascularization that results from diabetic and other retinopathies, and could be useful for inhibiting tumor-induced angiogenesis.

L2 ANSWER 18 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2004516411 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15361838
TITLE: Recombinant CD44-HABD is a novel and potent direct angiogenesis inhibitor enforcing endothelial cell-specific growth inhibition independently of hyaluronic acid binding.
AUTHOR: Pall Taavi; Gad Annica; Kasak Lagle; Drews Monika; Stromblad Staffan; Kogerman Priit
CORPORATE SOURCE: Department of Laboratory Medicine, Karolinska Institutet, Huddinge University Hospital F 46, Huddinge, 141 86 Huddinge, Sweden.
SOURCE: Oncogene, (2004 Oct 14) Vol. 23, No. 47, pp. 7874-81.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200411

ENTRY DATE: Entered STN: 19 Oct 2004
Last Updated on STN: 19 Dec 2004
Entered Medline: 29 Nov 2004

AB CD44 is the main cellular receptor for hyaluronic acid (HA). We previously found that overexpression of CD44 inhibited tumor growth of mouse fibrosarcoma cells in mice. Here, we show that soluble recombinant CD44 HA-binding domain (CD44-HABD) acts directly onto endothelial cells by inhibiting endothelial cell proliferation in a cell-specific manner. Consequently, soluble recombinant CD44-HABD also blocked angiogenesis in vivo in chick and mouse, and thereby inhibited tumor growth of various origins at very low doses (0.25 mg/kg x day). The antiangiogenic effect of CD44 is independent of its HA-binding capacity, since mutants deficient in HA binding still maintain their antiangiogenic and antiproliferative properties. Recombinant CD44-HABD represents a novel class of angiogenesis inhibitors based on a cell-surface receptor.

L2 ANSWER 19 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2004142256 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15035435
TITLE: Inhibition of bFGF/EGF-dependent endothelial cell proliferation by the hyaluronan-binding protease from human plasma.
AUTHOR: Etscheid Michael; Beer Nicole; Kress Julia Anne; Seitz Rainer; Dodt Johannes
CORPORATE SOURCE: Department of Hematology and Transfusion Medicine, Paul-Ehrlich-Institut, Federal Agency for Sera and Vaccines, Langen, Germany.. etsmi@pei.de
SOURCE: European journal of cell biology, (2004 Jan) Vol. 82, No. 12, pp. 597-604.
Journal code: 7906240. ISSN: 0171-9335.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 24 Mar 2004
Last Updated on STN: 3 Nov 2004
Entered Medline: 2 Nov 2004

AB Recently we identified a plasma serine protease with a high affinity to glycosaminoglycans like heparin or hyaluronic acid, termed hyaluronan-binding protease (HABP). Since glycosaminoglycans are found on cell surfaces and in the extracellular matrix a physiological role of this plasma protease in a pericellular environment was postulated. Here we studied the influence of HABP on the regulation of endothelial cell growth. We found that HABP efficiently prevented the basic fibroblast growth factor/epidermal growth factor (bFGF/EGF)-dependent proliferation of human umbilical vein endothelial cells. Proteolytic cleavage of adhesion molecules was found to be involved, but was not solely responsible for the anti-proliferative activity. Pre-treatment of growth factor-supplemented cell culture medium with HABP indicated that no direct contact between the active protease and cells was required for growth inhibition. In vitro studies revealed a growth factor-directed activity of HABP, resulting in complexation and partial hydrolysis and, thus, inactivation of basic fibroblast growth factor, a potent mitogen for endothelial cells. Heparin and heparan sulfate fully protected bFGF from complexation and cleavage by HABP, although these glycosaminoglycans are known to enhance the proteolytic activity of HABP. This finding suggested that free circulating bFGF rather than bFGF bound to heparan sulfate proteoglycans would be a physiologic substrate. In conclusion, down-regulation of bFGF-dependent endothelial cell growth represents an important mechanism through which HABP could control cell growth in physiologic or pathologic processes like angiogenesis,

wound healing or tumor development.

L2 ANSWER 20 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2002352509 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12095629
TITLE: Control of capillary formation by membrane-anchored extracellular inhibitor of phospholipase A(2).
AUTHOR: Chen W M; Soria J; Soria C; Krimsky M; Yedgar S
CORPORATE SOURCE: INSERM - EMI 99-12, Hotel Dieu, Paris, France.
SOURCE: FEBS letters, (2002 Jul 3) Vol. 522, No. 1-3, pp. 113-8. Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 4 Jul 2002
Last Updated on STN: 15 Aug 2002
Entered Medline: 14 Aug 2002

AB Secretory phospholipase A(2) (sPLA(2)) has been reported to be involved in cell proliferation in general and in endothelial cell migration, processes required for capillary formation. Subsequently, we examined the potential control of angiogenesis by sPLA(2) inhibition, using a cell-impermeable sPLA(2) inhibitor composed of N-derivatized phosphatidyl-ethanolamine linked to hyaluronic acid. This inhibitor effectively inhibits the proliferation and migration of human bone marrow endothelial cells in a dose-dependent manner, and suppresses capillary formation induced by growth factors involved in vascularization of tumors and of atherosclerotic plaques. It is proposed that sPLA(2) inhibition introduces a novel approach in the control of cancer development and atherosclerosis.

L2 ANSWER 21 OF 25 MEDLINE on STN
ACCESSION NUMBER: 1998074894 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9414083
TITLE: Hyaluronectin blocks the stimulatory effect of hyaluronan-derived fragments on endothelial cells during angiogenesis in vitro.
AUTHOR: Trochon V; Mabilat-Pragnon C; Bertrand P; Legrand Y; Soria J; Soria C; Delpech B; Lu H
CORPORATE SOURCE: INSERM U353, Institut d'Hematologie, Hopital Saint Louis, Paris, France.
SOURCE: FEBS letters, (1997 Nov 24) Vol. 418, No. 1-2, pp. 6-10. Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 30 Jan 1998
Last Updated on STN: 30 Jan 1998
Entered Medline: 16 Jan 1998

AB Hyaluronic acid (HA) is a glycosaminoglycan of the extracellular matrix. Its fragmentation by the hyaluronidase, secreted by tumor cells, facilitates tumor invasion and the HA degradation products generated stimulate angiogenesis. We report here that the HA-binding protein hyaluronectin (HN) inhibits the stimulatory effect of HA-derived fragments on the proliferation and migration of endothelial cells in vitro, and hampers the organization of endothelial cells into capillary-like structures. Since HN strongly inhibits endothelial cell adhesion to immobilized HA, it is postulated that HN acts by impairing the binding to endothelial cells of HA fragments generated by hyaluronidase, thereby neutralizing the effect of HA degradation products on angiogenesis. Our results

reveal a new mechanism by which the angiogenesis induced by HA fragments is modulated by HN.

L2 ANSWER 22 OF 25 MEDLINE on STN
ACCESSION NUMBER: 96353904 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8755562
TITLE: Expression of hyaluronidase by tumor cells induces angiogenesis in vivo.
AUTHOR: Liu D; Pearlman E; Diaconu E; Guo K; Mori H; Haqqi T; Markowitz S; Willson J; Sy M S
CORPORATE SOURCE: Institute of Pathology, Cancer Research Institute, School of Medicine, Case Western Reserve University, Cleveland, OH 44106, USA.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1996 Jul 23) Vol. 93, No. 15, pp. 7832-7.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19 Dec 1996
Last Updated on STN: 3 Mar 2000
Entered Medline: 29 Oct 1996
AB Hyaluronic acid is a proteoglycan present in the extracellular matrix and is important for the maintenance of tissue architecture. Depolymerization of hyaluronic acid may facilitate tumor invasion. In addition, oligosaccharides of hyaluronic acid have been reported to induce angiogenesis. We report here that a hyaluronidase similar to the one on human sperm is expressed by metastatic human melanoma, colon carcinoma, and glioblastoma cell lines and by tumor biopsies from patients with colorectal carcinomas, but not by tissues from normal colon. Moreover, angiogenesis is induced by hyaluronidase+ tumor cells but not hyaluronidase- tumor cells and can be blocked by an inhibitor of hyaluronidase. Tumor cells thus use hyaluronidase as one of the "molecular saboteurs" to depolymerize hyaluronic acid to facilitate invasion. As a consequence, breakdown products of hyaluronic acid can further promote tumor establishment by inducing angiogenesis. Hyaluronidase on tumor cells may provide a target for anti-neoplastic drugs.

L2 ANSWER 23 OF 25 MEDLINE on STN
ACCESSION NUMBER: 95255979 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7537724
TITLE: Angiogenesis: models and modulators.
AUTHOR: Cockerill G W; Gamble J R; Vadas M A
CORPORATE SOURCE: Hanson Center for Cancer Research, Institute of Medical and Veterinary Research, Adelaide, South Australia.
SOURCE: International review of cytology, (1995) Vol. 159, pp. 113-60. Ref: 277
Journal code: 2985180R. ISSN: 0074-7696.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 15 Jun 1995
Last Updated on STN: 29 Jan 1996
Entered Medline: 7 Jun 1995
AB Angiogenesis in vivo is distinguished by four stages: subsequent

to the transduction of signals to differentiate, stage 1 is defined as an altered proteolytic balance of the cell allowing it to digest through the surrounding matrix. These committed cells then proliferate (stage 2), and migrate (stage 3) to form aligned cords of cells. The final stage is the development of vessel patency (stage 4), generated by a coalescing of intracellular vacuoles. Subsequently, these structures anastamose and the initial flow of blood through the new vessel completes the process. We present and discuss how the available models most closely represent phases of in vivo angiogenesis. The enhancement of angiogenesis by hyaluronic acid fragments, transforming growth factor beta, tumor necrosis factor alpha, angiogenin, okadaic acid, fibroblast growth factor, interleukin 8, vascular endothelial growth factor, haptoglobin, and gangliosides, and the inhibition of the process by hyaluronic acid, estrogen metabolites, genestein, heparin, cyclosporin A, placental RNase inhibitor, steroids, collagen synthesis inhibitors, thrombospondin, fumagellin, and protamine are also discussed.

L2 ANSWER 24 OF 25 MEDLINE on STN
ACCESSION NUMBER: 89079402 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2462549
TITLE: Involvement of heparanase in tumor metastasis and angiogenesis.
AUTHOR: Vlodavsky I; Michaeli R I; Bar-Ner M; Fridman R; Horowitz A T; Fuks Z; Biran S
CORPORATE SOURCE: Sharett Institute of Oncology, Hadassah University Hospital, Jerusalem, Israel.
CONTRACT NUMBER: CA 30289 (NCI)
SOURCE: Israel journal of medical sciences, (1988 Sep-Oct) Vol. 24, No. 9-10, pp. 464-70.
Journal code: 0013105. ISSN: 0021-2180.
PUB. COUNTRY: Israel
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198902
ENTRY DATE: Entered STN: 8 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 8 Feb 1989

AB The capacity of various blood-borne cells, whether normal or malignant, to extravasate was found to correlate with heparanase-mediated degradation of HS in subendothelial ECM. This degradation was stimulated by proteases or plasminogen and inhibited by native heparin and by various modified nonanticoagulant species of heparin. These heparins also induced a marked reduction in tumor cell metastasis and autoimmune diseases in experimental animals. Heparanase-mediated degradation of HS in ECM also released EC growth factors that are stored in ECM, most likely by high affinity binding to HS. Such growth factors were extracted from subendothelial ECM synthesized in vitro and from basement membranes of the cornea in vivo, and are structurally and functionally related to bFGF;bFGF binds to ECM and is readily released by incubation with either HS, heparin or low MW heparin fragments as well as by various normal and malignant cells and by heparanase-mediated degradation of ECM HS. In contrast, there was little or no release of growth-promoting activity upon incubation of ECM with hyaluronic acid, chondroitin sulfate or chondroitinase ABC. A model is proposed suggesting that regulation of capillary growth and neovascular response may result from displacement of an angiogenic protein (bFGF) from its storage sites within basement membranes.

L2 ANSWER 25 OF 25 MEDLINE on STN
ACCESSION NUMBER: 88092358 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2447383
TITLE: Fibrin containing gels induce angiogenesis. Implications

for tumor stroma generation and wound healing.

AUTHOR: Dvorak H F; Harvey V S; Estrella P; Brown L F; McDonagh J; Dvorak A M
CORPORATE SOURCE: Department of Pathology, Beth Israel Hospital, Boston, Massachusetts.

CONTRACT NUMBER: CA-28741 (NCI)
CA-28834 (NCI)
CA-40624 (NCI)
SOURCE: Laboratory investigation; a journal of technical methods and pathology, (1987 Dec) Vol. 57, No. 6, pp. 673-86.
Journal code: 0376617. ISSN: 0023-6837.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198802
ENTRY DATE: Entered STN: 5 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 2 Feb 1988

AB Fibrin deposition is a consistent early event in solid tumors and healing wounds and precedes new blood vessel ingrowth in both. We now demonstrate that fibrin gels of themselves induce an angiogenic response in the absence of tumor cells or platelets. Angiogenesis was enhanced when certain chemoattractants or mitogens were included in the fibrin gel. Newly devised, inert plastic chambers with one porous surface were filled with varying contents and were implanted in the subcutaneous space of guinea pigs. Chambers filled with cross-linked homologous fibrin or plasma induced an angiogenic response within 4 days. Vessels entered chambers through the surface pores and flared out radially; angiogenesis was quantitated by point counting. Vessels were functional and matured along a gradient that proceeded from distal (least mature) to proximal. The intensity of the angiogenic response was enhanced when zymosan activated serum, an N-formylmethionine tripeptide, or platelet-derived growth factor was included in the fibrin matrix. Prior aldehyde fixation or boiling of fibrin-filled chambers inhibited angiogenesis, as did high concentrations of hyaluronic acid. Chambers filled with type I collagen or agarose did not induce new blood vessel formation, but addition of collagen did not reduce fibrin's capacity to initiate angiogenesis. The novel assay introduced here offers several advantages that should facilitate the study of angiogenesis. These include reproducibility, low background, objective and quantitative scoring, and the capacity to evaluate native molecules in animals of several species. Taken together, our findings strongly implicate fibrin or related proteins in the pathogenesis of angiogenesis and offer a new approach for elucidating the underlying molecular mechanisms.

L2 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:586488 CAPLUS
DOCUMENT NUMBER: 145:89926
TITLE: Pharmaceutical composition containing angiogenesis inhibitor for treating solid tumor
INVENTOR(S): Kong, Qingzhong; Sun, Juan
PATENT ASSIGNEE(S): Shandong Lanjin Biotech Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 14 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1686556	A	20051026	CN 2005-10042265	20050406

PRIORITY APPLN. INFO.: CN 2005-10042265 20050406

AB The title composition contains angiogenesis inhibitor or mixture of angiogenesis inhibitor and anticancer agent (nitrosourea compound) as active component. The angiogenesis inhibitor can be selected from one or more of carboxyamidotriazole, thalidomide, linomide, angiostatin, endostatin, etc. The topical sustained-release of effective components can reduce systemic toxic reaction, selectively increase the drug level at the tumor site, and improve the therapeutic effect of non-operative therapy such as chemotherapy and radiotherapy.

L2 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:586483 CAPLUS
DOCUMENT NUMBER: 145:130748
TITLE: Manufacture of drug composition containing angiogenesis inhibitor for treating tumor
INVENTOR(S): Kong, Qingzhong; Sun, Juan
PATENT ASSIGNEE(S): Shandong Lanjin Biotech Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 20 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1686546	A	20051026	CN 2005-10042264	20050406

PRIORITY APPLN. INFO.: CN 2005-10042264 20050406

AB The title composition contains tyrosine kinase inhibitor or a combination of tyrosine kinase inhibitor and nitrosourea antitumor agent as active component and auxiliary materials. The composition can effectively destroy tumor blood vessel, inhibit neovascularization, and promote penetration and diffusion of antitumor agents into the tumor tissues, therefore decreasing the tolerance of tumor tissues to nitrosourea antitumor agents. The auxiliary materials are composed of degradable and biocompatible polymers, which can achieve the sustained-release of antitumor agents specifically to tumor tissues, therefore decreasing the drug toxicity of whole body while maintaining necessary drug concentration on tumor tissues.

L2 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:591962 CAPLUS
DOCUMENT NUMBER: 143:91004
TITLE: Use of PSP64 and subfragments to suppress cell adhesion and migration, inhibit matrix metalloproteinase secretion, and treat cancer and

L2 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:586488 CAPLUS
DOCUMENT NUMBER: 145:89926
TITLE: Pharmaceutical composition containing angiogenesis inhibitor for treating solid tumor
INVENTOR(S): Kong, Qingzhong; Sun, Juan
PATENT ASSIGNEE(S): Shandong Lanjin Biotech Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 14 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1686556	A	20051026	CN 2005-10042265	20050406

PRIORITY APPLN. INFO.: CN 2005-10042265 20050406
AB The title composition contains angiogenesis inhibitor or mixture of angiogenesis inhibitor and anticancer agent (nitrosourea compound) as active component. The angiogenesis inhibitor can be selected from one or more of carboxyamidotriazole, thalidomide, linomide, angiostatin, endostatin, etc. The topical sustained-release of effective components can reduce systemic toxic reaction, selectively increase the drug level at the tumor site, and improve the therapeutic effect of non-operative therapy such as chemotherapy and radiotherapy.

L2 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:586483 CAPLUS
DOCUMENT NUMBER: 145:130748
TITLE: Manufacture of drug composition containing angiogenesis inhibitor for treating tumor
INVENTOR(S): Kong, Qingzhong; Sun, Juan
PATENT ASSIGNEE(S): Shandong Lanjin Biotech Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 20 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1686546	A	20051026	CN 2005-10042264	20050406

PRIORITY APPLN. INFO.: CN 2005-10042264 20050406
AB The title composition contains tyrosine kinase inhibitor or a combination of tyrosine kinase inhibitor and nitrosourea antitumor agent as active component and auxiliary materials. The composition can effectively destroy tumor blood vessel, inhibit neovascularization, and promote penetration and diffusion of antitumor agents into the tumor tissues, therefore decreasing the tolerance of tumor tissues to nitrosourea antitumor agents. The auxiliary materials are composed of degradable and biocompatible polymers, which can achieve the sustained-release of antitumor agents specifically to tumor tissues, therefore decreasing the drug toxicity of whole body while maintaining necessary drug concentration on tumor tissues.

L2 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:591962 CAPLUS
DOCUMENT NUMBER: 143:91004
TITLE: Use of PSP64 and subfragments to suppress cell adhesion and migration, inhibit matrix metalloproteinase secretion, and treat cancer and

other diseases

INVENTOR(S): Panchal, Chandra J.; Wu, Jinzi Jason; Beliveau, Richard; Ruiz, Marcia; Garde, Seema; Annabi, Borhane; Lamy, Sylvie; Bouzeghrane, Mounia; Daigneault, Luc; Hawkins, Robert

PATENT ASSIGNEE(S): Can.

SOURCE: U.S. Pat. Appl. Publ., 59 pp., Cont.-in-part of U.S. Ser. No. 948,229.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005147601	A1	20050707	US 2004-4270	20041202
CA 2441695	AA	20050326	CA 2003-2441695	20030926
US 2005096273	A1	20050505	US 2004-948229	20040924
WO 2005118623	A1	20051215	WO 2005-CA430	20050321

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

CA 2003-2441695	A	20030926
US 2004-948229	A2	20040924
US 2004-857358	A	20040601
US 2004-4270	A	20041202
US 2004-4273	A	20041202

AB Matrix metalloproteinases (MMPs) play an important role in morphogenesis, angiogenesis, wound healing, and in certain disorders such as rheumatoid arthritis, tumor invasion and metastasis. MMPs are thought to be regulated by a variety of cytokines, growth factors, hormones and phorbol esters. This regulation occurs on three levels; alteration of gene expression, activation of the latent zymogen and inhibition by the tissue inhibitors of metalloproteinases (TIMP). We report here a new agent that regulates the level of MMPs, i.e., prostate secretory protein PSP94. Thus, PCK3145, a pentadecapeptide derived from PSP94, significantly decreased levels of MMP-9 in the blood of patients with metastatic adenocarcinoma of the prostate. A derivative of PCK3145 in which the 3 cysteine SH groups were acetaminomethylated, suppressed secretion of MMP from Mat-LyLu cells. This derivs. also decreased U-87 cell adhesion to hyaluronic acid as well as U-87 cell migration. Further effects of the PSP94 peptide derivative were increased CD44 cell surface shedding and induction of RhoA protein expression.

L2 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:839781 CAPLUS

DOCUMENT NUMBER: 142:106540

TITLE: Recombinant CD44-HABD is a novel and potent direct angiogenesis inhibitor enforcing endothelial cell-specific growth inhibition independently of hyaluronic acid binding

AUTHOR(S): Paell, Taavi; Gad, Annica; Kasak, Lagle; Drews, Monika; Stroemblad, Staffan; Kogerman, Priit

CORPORATE SOURCE: Karolinska Institutet, Department of Laboratory

other diseases

INVENTOR(S): Panchal, Chandra J.; Wu, Jinzi Jason; Beliveau, Richard; Ruiz, Marcia; Garde, Seema; Annabi, Borhane; Lamy, Sylvie; Bouzeghrane, Mounia; Daigneault, Luc; Hawkins, Robert

PATENT ASSIGNEE(S): Can.

SOURCE: U.S. Pat. Appl. Publ., 59 pp., Cont.-in-part of U.S. Ser. No. 948,229.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005147601	A1	20050707	US 2004-4270	20041202
CA 2441695	AA	20050326	CA 2003-2441695	20030926
US 2005096273	A1	20050505	US 2004-948229	20040924
WO 2005118623	A1	20051215	WO 2005-CA430	20050321

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

CA 2003-2441695	A	20030926
US 2004-948229	A2	20040924
US 2004-857358	A	20040601
US 2004-4270	A	20041202
US 2004-4273	A	20041202

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L2 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:839781 CAPLUS

DOCUMENT NUMBER: 142:106540

TITLE: Recombinant CD44-HABD is a novel and potent direct angiogenesis inhibitor enforcing endothelial cell-specific growth inhibition independently of hyaluronic acid binding

AUTHOR(S): Paell, Taavi; Gad, Annica; Kasak, Lagle; Drews, Monika; Stroemblad, Staffan; Kogerman, Priit

CORPORATE SOURCE: Karolinska Institutet, Department of Laboratory

Medicine, Huddinge University Hospital F 46, Huddinge, 141 86, Swed.
SOURCE: Oncogene (2004), 23(47), 7874-7881
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CD44 is the main cellular receptor for hyaluronic acid (HA). We previously found that overexpression of CD44 inhibited tumor growth of mouse fibrosarcoma cells in mice. Here, we show that soluble recombinant CD44 HA-binding domain (CD44-HABD) acts directly onto endothelial cells by inhibiting endothelial cell proliferation in a cell-specific manner. Consequently, soluble recombinant CD44-HABD also blocked angiogenesis in vivo in chick and mouse, and thereby inhibited tumor growth of various origins at very low doses (0.25 mg/kg + day). The antiangiogenic effect of CD44 is independent of its HA-binding capacity, since mutants deficient in HA binding still maintain their antiangiogenic and antiproliferative properties. Recombinant CD44-HABD represents a novel class of angiogenesis inhibitors based on a cell-surface receptor.
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:727145 CAPLUS
DOCUMENT NUMBER: 141:347043
TITLE: Brain hyaluronan binding protein inhibits tumor growth
AUTHOR(S): Gao, Feng; Cao, Man-lin; Wang, Lei
CORPORATE SOURCE: Department of Clinical Laboratory, Sixth People's Hospital, Medical School, Shanghai Jiaotong University, Shanghai, 200233, Peop. Rep. China
SOURCE: Chinese Medical Journal (Beijing, China, English Edition) (2004), 117(7), 1072-1078
CODEN: CMJODS; ISSN: 0366-6999
PUBLISHER: Chinese Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Great efforts have been made to search for the angiogenic inhibitors in avascular tissues. Several proteins isolated from cartilage have been proved to have anti-angiogenic or antitumor effects. Because cartilage contains a great amount of hyaluronic acid (HA) oligosaccharides and abundant HA binding proteins (HABP), therefore, we speculated that HABP might be one of the factors regulating vascularization in cartilage or anti-angiogenesis in tumors. The purpose of this research was to evaluable the effects of hyaluronan binding protein on inhibiting tumor growth both in vivo and vitro. A unique protein termed human brain hyaluronan (HA) binding protein (b-HABP) was cloned from human brain cDNA library. MDA-435 human breast cancer cell line was chosen as a transfectant. The in vitro underlying mechanisms were investigated by determining the possibilities of MDA-435/b-HABP colony formation on soft agar, the effects of the transfectant on the proliferation of endothelial cells and the expression levels of caspase 3 and FasL from MDA-435/b-HABP. The in vivo study included tumor growth on the chorioallantoic membrane (CAM) of chicken embryos and nude mice. Colony formation assay revealed that the colonies formed by MDA-435/b-HABP were greatly reduced compared to mock transfectants. The conditioned media from MDA-435/b-HABP inhibited the growth of endothelial cells in culture. Caspase 3 and FasL expressions were induced by MDA-435/b-HABP. The size of tumors of MDA-435/b-HABP in both CAM and nude mice was much smaller than that of MDA-435 alone. Human brain hyaluronan binding protein (b-HABP) may represent a new kind of naturally existing anti-tumor substance. This brain-derived glycoprotein may block

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CODEN: ONCNES; ISSN: 0950-9232
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DOCUMENT TYPE: Journal
LANGUAGE: English
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SOURCE: Chinese Medical Journal (Beijing, China, English Edition) (2004), 117(7), 1072-1078
CODEN: CMJODS; ISSN: 0366-6999
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DOCUMENT TYPE: Journal
LANGUAGE: English
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tumor growth by inducing apoptosis of cancer cells or by decreasing angiogenesis in tumor tissue via inhibiting proliferation of endothelial cells.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:342426 CAPLUS
DOCUMENT NUMBER: 141:325311
TITLE: Inhibition of bFGF/EGF-dependent endothelial cell proliferation by the hyaluronan-binding protease from human plasma
AUTHOR(S): Etscheid, Michael; Beer, Nicole; Kress, Julia Anne; Seitz, Rainer; Dodt, Johannes
CORPORATE SOURCE: Department of Hematology and Transfusion Medicine, Paul-Ehrlich-Institut, Federal Agency for Sera and Vaccines, Langen, D-63225, Germany
SOURCE: European Journal of Cell Biology (2004), 82(12), 597-604
CODEN: EJCBDN; ISSN: 0171-9335
PUBLISHER: Elsevier GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recently we identified a plasma serine protease with a high affinity to glycosaminoglycans like heparin or hyaluronic acid, termed hyaluronan-binding protease (HABP). Since glycosaminoglycans are found on cell surfaces and in the extracellular matrix a physiol. role of this plasma protease in a pericellular environment was postulated. Here we studied the influence of HABP on the regulation of endothelial cell growth. We found that HABP efficiently prevented the basic fibroblast growth factor/epidermal growth factor (bFGF/EGF)-dependent proliferation of human umbilical vein endothelial cells. Proteolytic cleavage of adhesion mols. was found to be involved, but was not solely responsible for the anti-proliferative activity. Pre-treatment of growth factor-supplemented cell culture medium with HABP indicated that no direct contact between the active protease and cells was required for growth inhibition. In vitro studies revealed a growth factor-directed activity of HABP, resulting in complexation and partial hydrolysis and, thus, inactivation of basic fibroblast growth factor, a potent mitogen for endothelial cells. Heparin and heparan sulfate fully protected bFGF from complexation and cleavage by HABP, although these glycosaminoglycans are known to enhance the proteolytic activity of HABP. This finding suggested that free circulating bFGF rather than bFGF bound to heparan sulfate proteoglycans would be a physiol. substrate. In conclusion, down-regulation of bFGF-dependent endothelial cell growth represents an important mechanism through which HABP could control cell growth in physiol. or pathol. processes like angiogenesis, wound healing or tumor development.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:551368 CAPLUS
DOCUMENT NUMBER: 139:122818
TITLE: Biomaterials based on hyaluronic acid for the anti-angiogenic therapy in the treatment of tumors
INVENTOR(S): Fusenig, Norbert E.; Stark, Hans-Juergen; Willhauck, Michael; Pavesio, Alessandra
PATENT ASSIGNEE(S): Fidia Farmaceutici S.p.A., Italy; Deutsches Krebsforschungszentrum (DKFZ)
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

tumor growth by inducing apoptosis of cancer cells or by decreasing angiogenesis in tumor tissue via inhibiting proliferation of endothelial cells.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

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CORPORATE SOURCE: Department of Hematology and Transfusion Medicine, Paul-Ehrlich-Institut, Federal Agency for Sera and Vaccines, Langen, D-63225, Germany
SOURCE: European Journal of Cell Biology (2004), 82(12), 597-604
CODEN: EJCBDN; ISSN: 0171-9335
PUBLISHER: Elsevier GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

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PATENT ASSIGNEE(S): Fidia Farmaceutici S.p.A., Italy; Deutsches Krebsforschungszentrum (DKFZ)
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057203	A2	20030717	WO 2003-EP78	20030107
WO 2003057203	A3	20031231		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2472880	AA	20030717	CA 2003-2472880	20030107
AU 2003201618	A1	20030724	AU 2003-201618	20030107
EP 1463541	A2	20041006	EP 2003-700315	20030107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005524619	T2	20050818	JP 2003-557561	20030107
US 2005037049	A1	20050217	US 2004-501030	20040812
PRIORITY APPLN. INFO.:			IT 2002-PD3 A	20020111
			WO 2003-EP78 W	20030107

AB The use in the medical-surgical field of biomaterials based on hyaluronic acid derivs., optionally in association with natural, synthetic or semi-synthetic biopolymers, for suppressing the angiogenic process associated with tumor proliferation (in primary and secondary tumors) is disclosed. For example, the Hyaff 11-based biomaterial proved able to modulate/inhibit the angiogenic process related to vascularization of the cancerous epithelium.

L2 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:286155 CAPLUS
DOCUMENT NUMBER: 139:211727
TITLE: Influences of hyaluronic acid binding protein on expressions of human cancer cells cyclin E and p27kip1
AUTHOR(S): Gao, Feng; Sun, Tinglu; Cao, Manlin; Zhang, Lurong; Underhill, C. B.
CORPORATE SOURCE: Department of Clinical Laboratory, Shanghai Sixth People's Hospital, Shanghai, 200233, Peop. Rep. China
SOURCE: Shanghai Yixue (2002), 25(9), 581-583
CODEN: SIHSD8; ISSN: 0253-9934
PUBLISHER: Shanghai Yixue Bianji Weiyuanhui
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The influences of hyaluronic acid binding protein (HABP) on expressions of human cancer cells cyclin E and p27kip1 and adult bovine arterial endothelial cells (ABAE) p27kip1 were studied. Full length cDNA of human brain hyaluronic acid binding protein (hbHABP) was transfected into human breast cancer cell line (MDA435) and prostatic cancer cell line (TSU). Cyclin E and p27kip1 expression from these transfectants were detected by Western blot. In addition, conditioned medium (CM) from these transfectants was added to the cultured ABAE, and the p27kip1 expression was also determined The expression of cyclin E was decreased and that of p27kip1 was markedly increased in both MDA435 and TSU cells. There expression of p27kip1 in ABAE cells was increased in the presence of the CM. The hbHABP may have the inhibitory effects on human breast cancer and prostate cancer cells growth via the following mechanisms: from inhibiting cancer cells cyclin E expression and inducing inhibitor of

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057203	A2	20030717	WO 2003-EP78	20030107
WO 2003057203	A3	20031231		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2472880	AA	20030717	CA 2003-2472880	20030107
AU 2003201618	A1	20030724	AU 2003-201618	20030107
EP 1463541	A2	20041006	EP 2003-700315	20030107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005524619	T2	20050818	JP 2003-557561	20030107
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PRIORITY APPLN. INFO.:			IT 2002-PD3 A	20020111
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CORPORATE SOURCE: Department of Clinical Laboratory, Shanghai Sixth People's Hospital, Shanghai, 200233, Peop. Rep. China
SOURCE: Shanghai Yixue (2002), 25(9), 581-583
CODEN: SIHSD8; ISSN: 0253-9934
PUBLISHER: Shanghai Yixue Bianji Weiyuanhui
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

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cyclin-dependent kinase p27kip1 expression, inhibiting tumor angiogenesis by increasing endothelial cells p27kip1 expression.

L2 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:173455 CAPLUS
DOCUMENT NUMBER: 138:198601
TITLE: New drug recombinant CD44 protein
INVENTOR(S): Stroemblad, Staffan; Kogerman, Priit; Paell, Taavi
PATENT ASSIGNEE(S): Swed.
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003018044	A1	20030306	WO 2002-SE1531		20020826
WO 2003018044	C1	20040624			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2458565	AA	20030306	CA 2002-2458565		20020826
EP 1418931	A1	20040519	EP 2002-760977		20020826
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
CN 1561223	A	20050105	CN 2002-819275		20020826
JP 2005525995	T2	20050902	JP 2003-522561		20020826
US 2005054593	A1	20050310	US 2004-487620		20040524
PRIORITY APPLN. INFO.:			SE 2001-2823	A	20010824
			US 2001-314971P	P	20010824
			WO 2002-SE1531	W	20020826

AB CD44, the receptor for hyaluronic acid, has complex functions in cellular physiol., cell migration and tumor metastasis. The inventors have previously found that human CD44 receptor overexpression in mouse fibrosarcoma cells inhibits s.c. tumor growth in mice. Here it is demonstrated that a tumor growth inhibitory effect of CD44 is caused by block of angiogenesis. Furthermore, the inventors have found that soluble recombinant CD44 hyaluronic acid binding domain (CD44HABD) inhibits angiogenesis in vivo in cLick and mouse and thereby inhibits human tumor growth of various origins. The anti-angiogenic effect of CD44-HABD is independent of hyaluronic acid (HA) binding, since non-HA-binding mutants of CD44HABD still maintain anti-angiogenic properties. The invention discloses soluble CD44 recombinant proteins as a novel class of angiogenesis inhibitors based on targeting of vascular cell surface receptor. A method of block of angiogenesis and treatment of human tumors using recombinant CD44 proteins as well as their analogs is disclosed. As a further embodiment of the invention, methods for screening for new drug targets using CD44 recombinant proteins and their analogs is presented.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

cyclin-dependent kinase p27kip1 expression, inhibiting tumor angiogenesis by increasing endothelial cells p27kip1 expression.

L2 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:173455 CAPLUS
DOCUMENT NUMBER: 138:198601
TITLE: New drug recombinant CD44 protein
INVENTOR(S): Stroemblad, Staffan; Kogerman, Priit; Paell, Taavi
PATENT ASSIGNEE(S): Swed.
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003018044	A1	20030306	WO 2002-SE1531		20020826
WO 2003018044	C1	20040624			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2458565	AA	20030306	CA 2002-2458565		20020826
EP 1418931	A1	20040519	EP 2002-760977		20020826
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
CN 1561223	A	20050105	CN 2002-819275		20020826
JP 2005525995	T2	20050902	JP 2003-522561		20020826
US 2005054593	A1	20050310	US 2004-487620		20040524
PRIORITY APPLN. INFO.:			SE 2001-2823	A	20010824
			US 2001-314971P	P	20010824
			WO 2002-SE1531	W	20020826

AB CD44, the receptor for hyaluronic acid, has complex functions in cellular physiol., cell migration and tumor metastasis. The inventors have previously found that human CD44 receptor overexpression in mouse fibrosarcoma cells inhibits s.c. tumor growth in mice. Here it is demonstrated that a tumor growth inhibitory effect of CD44 is caused by block of angiogenesis. Furthermore, the inventors have found that soluble recombinant CD44 hyaluronic acid binding domain (CD44HABD) inhibits angiogenesis in vivo in cLick and mouse and thereby inhibits human tumor growth of various origins. The anti-angiogenic effect of CD44-HABD is independent of hyaluronic acid (HA) binding, since non-HA-binding mutants of CD44HABD still maintain anti-angiogenic properties. The invention discloses soluble CD44 recombinant proteins as a novel class of angiogenesis inhibitors based on targeting of vascular cell surface receptor. A method of block of angiogenesis and treatment of human tumors using recombinant CD44 proteins as well as their analogs is disclosed. As a further embodiment of the invention, methods for screening for new drug targets using CD44 recombinant proteins and their analogs is presented.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:495934 CAPLUS
DOCUMENT NUMBER: 138:130798
TITLE: Control of capillary formation by membrane-anchored extracellular inhibitor of phospholipase A2
AUTHOR(S): Chen, W. M.; Soria, J.; Soria, C.; Krimsky, M.; Yedgar, S.
CORPORATE SOURCE: INSERM - EMI 99-12, Hotel Dieu, Paris, INSERM -EMI 99-12, Fr.
SOURCE: FEBS Letters (2002), 522(1-3), 113-118
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Secretory phospholipase A2 (sPLA2) has been reported to be involved in cell proliferation in general and in endothelial cell migration, processes required for capillary formation. Subsequently, we examined the potential control of angiogenesis by sPLA2 inhibition, using a cell-impermeable sPLA2 inhibitor composed of N-derivatized phosphatidyl-ethanolamine linked to hyaluronic acid. This inhibitor effectively inhibits the proliferation and migration of human bone marrow endothelial cells in a dose-dependent manner, and suppresses capillary formation induced by growth factors involved in vascularization of tumors and of atherosclerotic plaques. It is proposed that sPLA2 inhibition introduces a novel approach in the control of cancer development and atherosclerosis.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:666590 CAPLUS
DOCUMENT NUMBER: 133:242678
TITLE: Angiogenesis inhibition with pharmaceutical containing reaction products of hyaluronic acid, CM-cellulose and carbodiimide
INVENTOR(S): Moulton, Steven
PATENT ASSIGNEE(S): Trustees of Boston University, USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000054762	A2	20000921	WO 2000-US6819	20000315
WO 2000054762	A3	20010308		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2365767	AA	20000921	CA 2000-2365767	20000315
EP 1162984	A2	20011219	EP 2000-917975	20000315
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6472379	B1	20021029	US 2000-525402	20000315
JP 2002539157	T2	20021119	JP 2000-604838	20000315
US 2002169144	A1	20021114	US 2002-147204	20020516

L2 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:495934 CAPLUS
DOCUMENT NUMBER: 138:130798
TITLE: Control of capillary formation by membrane-anchored extracellular inhibitor of phospholipase A2
AUTHOR(S): Chen, W. M.; Soria, J.; Soria, C.; Krimsky, M.; Yedgar, S.
CORPORATE SOURCE: INSERM - EMI 99-12, Hotel Dieu, Paris, INSERM -EMI 99-12, Fr.
SOURCE: FEBS Letters (2002), 522(1-3), 113-118
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Secretory phospholipase A2 (sPLA2) has been reported to be involved in cell proliferation in general and in endothelial cell migration, processes required for capillary formation. Subsequently, we examined the potential control of angiogenesis by sPLA2 inhibition, using a cell-impermeable sPLA2 inhibitor composed of N-derivatized phosphatidyl-ethanolamine linked to hyaluronic acid. This inhibitor effectively inhibits the proliferation and migration of human bone marrow endothelial cells in a dose-dependent manner, and suppresses capillary formation induced by growth factors involved in vascularization of tumors and of atherosclerotic plaques. It is proposed that sPLA2 inhibition introduces a novel approach in the control of cancer development and atherosclerosis.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:666590 CAPLUS
DOCUMENT NUMBER: 133:242678
TITLE: Angiogenesis inhibition with pharmaceutical containing reaction products of hyaluronic acid, CM-cellulose and carbodiimide
INVENTOR(S): Moulton, Steven
PATENT ASSIGNEE(S): Trustees of Boston University, USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000054762	A2	20000921	WO 2000-US6819	20000315
WO 2000054762	A3	20010308		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2365767	AA	20000921	CA 2000-2365767	20000315
EP 1162984	A2	20011219	EP 2000-917975	20000315
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6472379	B1	20021029	US 2000-525402	20000315
JP 2002539157	T2	20021119	JP 2000-604838	20000315
US 2002169144	A1	20021114	US 2002-147204	20020516

PRIORITY APPLN. INFO.: US 1999-124703P P 19990315
US 2000-525402 A1 20000315
WO 2000-US6819 W 20000315

AB Angiogenesis is inhibited by the local administration of a pharmaceutical preparation formed from the reaction of hyaluronic acid, CM-cellulose and a carbodiimide. The preparation, which can be in the form of a film or a gel, is advantageously applied directly to the site of a tumor, such as a cancerous tumor, used in conjunction with other chemotherapeutic techniques, or used to treat a chronic inflammatory condition, such as rheumatoid arthritis, endometriosis, arteriosclerosis, intimal hyperplasia, proliferative retinopathy, and the like. Seprafilm inhibited the growth of vessels and the formation of adhesions in mice.

L2 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:594961 CAPLUS
DOCUMENT NUMBER: 131:209122
TITLE: Metastatin and hyaluronate-binding proteins and methods of use
INVENTOR(S): Green, Shawn J.; Underhill, Charles B.
PATENT ASSIGNEE(S): Entremed, Inc., USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9945942	A1	19990916	WO 1999-US5498	19990312
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2324624	AA	19990916	CA 1999-2324624	19990312
AU 9930856	A1	19990927	AU 1999-30856	19990312
EP 1064011	A1	20010103	EP 1999-912488	19990312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1998-77898P P 19980313
US 1998-108124P P 19981112
WO 1999-US5498 W 19990312

AB Compns. comprising hyaluronate (HA)-binding proteins and peptides are provided as well as methods of using the HA-binding proteins and peptides to inhibit cancer and angiogenesis-dependent diseases. In a preferred embodiment, the hyaluronic acid-binding link module is metastatin protein, an approx. 38 kDa inhibitor of tumor growth and tumor metastasis.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

PRIORITY APPLN. INFO.: US 1999-124703P P 19990315
US 2000-525402 A1 20000315
WO 2000-US6819 W 20000315

AB Angiogenesis is inhibited by the local administration of a pharmaceutical preparation formed from the reaction of hyaluronic acid, CM-cellulose and a carbodiimide. The preparation, which can be in the form of a film or a gel, is advantageously applied directly to the site of a tumor, such as a cancerous tumor, used in conjunction with other chemotherapeutic techniques, or used to treat a chronic inflammatory condition, such as rheumatoid arthritis, endometriosis, arteriosclerosis, intimal hyperplasia, proliferative retinopathy, and the like. Seprafilm inhibited the growth of vessels and the formation of adhesions in mice.

L2 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:594961 CAPLUS
DOCUMENT NUMBER: 131:209122
TITLE: Metastatin and hyaluronate-binding proteins and methods of use
INVENTOR(S): Green, Shawn J.; Underhill, Charles B.
PATENT ASSIGNEE(S): Entremed, Inc., USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9945942	A1	19990916	WO 1999-US5498	19990312
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2324624	AA	19990916	CA 1999-2324624	19990312
AU 9930856	A1	19990927	AU 1999-30856	19990312
EP 1064011	A1	20010103	EP 1999-912488	19990312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1998-77898P P 19980313
US 1998-108124P P 19981112
WO 1999-US5498 W 19990312

AB Compns. comprising hyaluronate (HA)-binding proteins and peptides are provided as well as methods of using the HA-binding proteins and peptides to inhibit cancer and angiogenesis-dependent diseases. In a preferred embodiment, the hyaluronic acid-binding link module is metastatin protein, an approx. 38 kDa inhibitor of tumor growth and tumor metastasis.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:387785 CAPLUS
DOCUMENT NUMBER: 127:63472
TITLE: CD44: structure, function, and association with the malignant process
AUTHOR(S): Naor, David; Sionov, Ronit Vogt; Ish-Shalom, Dvorah
CORPORATE SOURCE: The Lautenberg Center for General and Tumor Immunology, The Hebrew University-Hadassah Medical School, Jerusalem, 91120, Israel
SOURCE: Advances in Cancer Research (1997), 71, 241-319
CODEN: ACRSAJ; ISSN: 0065-230X
PUBLISHER: Academic
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 388 refs. CD44 is a ubiquitous multi-structural and multifunctional cell surface adhesion mol. involved in cell-cell and cell-matrix interactions. Twenty exons are involved in the genomic organization of this mol. The first five and the last 5 exons are constant, whereas the 10 exons located between these regions are subjected to alternative splicing, resulting in the generation of a variable region. Differential utilization of the 10 variable region exons, as well as variations in N-glycosylation, O-glycosylation, and glycosaminoglycanation (by heparan sulfate or chondroitin sulfate), generate multiple isoforms (at least 20 are known) of different mol. sizes (85-230 kDa). The smallest CD44 mol. (85-95 kDa), which lacks the entire variable region, is standard CD44 (CD44s). As it is expressed mainly on cells of lymphohematopoietic origin, CD44s is also known as hematopoietic CD44 (CD44H). CD44s is a single-chain mol. composed of a distal extracellular domain (containing the ligand-binding sites), a membrane-proximal region, a transmembrane-spanning domain, and a cytoplasmic tail. The mol. sequence (with the exception of the membrane-proximal region) displays high interspecies homol. After immunol. activation, T lymphocytes and other leukocytes transiently upregulate CD44 isoforms expressing variant exons (designated CD44v). A CD44 isoform containing the last 3 exon products of the variable region (CD44V8-10, also known as epithelial CD44 or CD44E), is preferentially expressed on epithelial cells. The longest CD44 isoform expressing in tandem eight exons of the variable region (CD44V3-10) was detected in keratinocytes. Hyaluronic acid (HA), an important component of the extracellular matrix (ECM), is the principal, but by no means the only, ligand of CD44. Other CD44 ligands include the ECM components collagen, fibronectin, laminin, and chondroitin sulfate. Mucosal addressin, serglycin, osteopontin, and the class II invariant chain (Ii) are addnl., ECM-unrelated, ligands of the mol. In many, but not in all cases, CD44 does not bind HA unless it is stimulated by phorbol esters, activated by agonistic anti-CD44 antibody, or deglycosylated (e.g., by tunicamycin). CD44 is a multifunctional receptor involved in cell-cell and cell-ECM interactions, cell traffic, lymph node homing, presentation of chemokines and growth factors to traveling cells, and transmission of growth signals. CD44 also participates in the uptake and intracellular degradation of HA, as well as in transmission of signals mediating hematopoiesis and apoptosis. Many cancer cell types as well as their metastases express high levels of CD44. Where-as some tumors, such as gliomas, exclusively express standard CD44, other neoplasms, including gastrointestinal cancer, bladder cancer, uterine cervical cancer, breast cancer and non-Hodgkin's lymphomas, also express CD44 variants. Hence CD44, particularly its variants, may be used as diagnostic or prognostic markers of at least some human malignant diseases. Furthermore, it has been shown in animal models that injection of reagents interfering with CD44-ligand interaction (e.g., CD44s- or CD44v-specific antibodies) inhibit local tumor growth and metastatic spread. These findings suggest that CD44 may confer a growth advantage on some neoplastic cells and, therefore, could be used as a target for cancer therapy. It is hoped that identification of CD44

variants expressed on cancer but not on normal cells will lead to the development of anti-CD44 reagents restricted to the neoplastic growth.

REFERENCE COUNT: 382 THERE ARE 382 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:253139 CAPLUS
DOCUMENT NUMBER: 118:253139
TITLE: CD44 antibody stimulates adhesion of peripheral blood T cells to keratinocytes through the leukocyte function-associated antigen-1/intercellular adhesion molecule-1 pathway
AUTHOR(S): Bruynzeel, Ineke; Koopman, Gerrit; van der Raaij, Liesbeth M. H.; Pals, Steven T.; Willemze, Rein
CORPORATE SOURCE: Dep. Dermatol., Free Univ. Hosp., Amsterdam, 1081 HV, Neth.
SOURCE: Journal of Investigative Dermatology (1993), 100(4), 424-8
CODEN: JIDEAE; ISSN: 0022-202X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Close contact between T lymphocytes and keratinocytes is an important feature of many inflammatory skin diseases. iN vitro studies showed that simulation of keratinocytes with interferon-γ or tumor necrosis factor-α and of T cells with phorbol esters results in a leukocyte function-associated antigen (LFA)-1/intercellular adhesion mol. (ICAM)-1-mediated adhesion. The present study was performed to investigate the role of the CD44 mol. in keratinocyte/T-cell binding. The CD44 class of lymphocyte adhesion receptors is involved in lymphocyte binding to high endothelial venules and to extracellular matrix compds. and is therefore important in lymphocyte recirculation and homing. Moreover, CD44 can act as a co-stimulating signal in T-cell activation and promotes homotypic adhesion of in vitro cultured CD3-stimulated T cells. Using a cell adhesion assay a sixfold increase in T-cell/keratinocyte adhesion was found after pre-incubating the T cells with anti-CD44. This increased adhesion was found to require an intact cytoskeleton, to be energy and magnesium dependent, and could be completely inhibited by anti-LFA-1 and anti-ICAM-1. Pretreatment of T cells with hyaluronic acid, a ligand for CD44 and an extracellular matrix compound in the dermis and epidermis, did not affect T-cell/keratinocyte adhesion.

L12 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:30845 CAPLUS
DOCUMENT NUMBER: 112:30845
TITLE: Effects of thyroid-stimulating hormone and phorbol ester on glycosaminoglycan synthesis in porcine thyroid epithelial cells in primary culture
AUTHOR(S): Wegrowski, J.; Bellon, G.; Haye, B.; Borel, J. P.
CORPORATE SOURCE: Lab. Biochim., Fac. Med., Reims, 51095, Fr.
SOURCE: Cell Biology International Reports (1989), 13(10), 881-90
CODEN: CBRPDS; ISSN: 0309-1651
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of TSH and of a tumor promoter (12-O-tetradecanoyl-phorbol-13-acetate) on glycosaminoglycan (GAG) synthesis were studied in porcine thyroid epithelial cells in primary culture. TSH is known to involve a cAMP mechanism and phorbol ester to act by the protein kinase C pathway. Chronic treatment of cells with TSH increased the synthesis of heparan sulfate associated with the cell layer and hyaluronic acid in the culture medium. Phorbol ester increased the radioactivity (from [3H]glucosamine and

[35S]sulfate) of total GAGs in the culture medium but had no effect on GAGs associated with the cell layer. It inhibited the pos. effect of TSH on heparan sulfate synthesis. In thyroid epithelial cells, the synthesis of the GAGs associated with the cell layer and those secreted into the culture medium are evidently regulated by different intracellular mechanisms.

L12 ANSWER 10 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2006255644 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16678050
TITLE: HYTAD1-p20: a new paclitaxel-hyaluronic acid hydrosoluble bioconjugate for treatment of superficial bladder cancer.
AUTHOR: Rosato Antonio; Banzato Alessandra; De Luca Gilda; Renier Davide; Bettella Fabio; Pagano Claudio; Esposito Giovanni; Zanovello Paola; Bassi PierFrancesco
CORPORATE SOURCE: Department of Oncology and Surgical Sciences, Oncology Section, University of Padua, Padua, Italy.. antonio.rosato@unipd.it
SOURCE: Urologic oncology, (2006 May-Jun) Vol. 24, No. 3, pp. 207-15.
Journal code: 9805460. ISSN: 1078-1439.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200610
ENTRY DATE: Entered STN: 9 May 2006
Last Updated on STN: 20 Oct 2006
Entered Medline: 19 Oct 2006

AB OBJECTIVE: To report the development of a new water-soluble paclitaxel-hyaluronic acid bioconjugate, HYTAD1-p20, for intravesical treatment of superficial bladder cancer. MATERIALS AND METHODS: HYTAD1-p20 was synthesized by carboxyl esterification of hyaluronic acid with paclitaxel, and its physicochemical and biologic properties were characterized. RESULTS: Paclitaxel loading was optimized at 20% w/w; this procedure increased by 500-fold the paclitaxel concentration in the resulting water-soluble biomaterial. In vitro, HYTAD1-p20 exerted a much higher dose-dependent inhibitory effect against RT-4 and RT-112/84 bladder carcinoma cell growth than that of free drug, and directly interacted with CD44 expressed by bladder tumor cells. In vivo, results of pharmacokinetic studies performed in mice after bladder catheterization and intravesical instillation of HYTAD1-p20 disclosed that drug leakage was negligible during a 2-hour analysis. Histologic examination of drug-instilled bladders revealed that HYTAD1-p20 was extremely well tolerated, while paclitaxel alone produced mucosal disruption and submucosal infiltration of inflammatory cells. Treatment of severe combined immunodeficient mice bearing subcutaneous RT-112/84 tumors with maximum tolerated doses of bioconjugate or paclitaxel showed that HYTAD1-p20 exerted a therapeutic activity comparable to that of free drug. CONCLUSIONS: These data suggest that HYTAD1-p20 significantly improved results obtained with conventional paclitaxel in terms of hydrosolubility, in vitro activity against human bladder cancer cells, and in vivo biocompatibility. This bioconjugate is a potentially useful treatment for superficial urothelial malignancy.

L12 ANSWER 11 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2005115084 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15746573
TITLE: Hyaluronic acid butyric esters in cancer therapy.
AUTHOR: Speranza Annalisa; Pellizzaro Cinzia; Coradini Danila
CORPORATE SOURCE: Unit of Biomolecular Determinants in Prognosis and Therapy, Experimental Department, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy.

SOURCE: Anti-cancer drugs, (2005 Apr) Vol. 16, No. 4, pp. 373-9.
Ref: 32
Journal code: 9100823. ISSN: 0959-4973.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200507
ENTRY DATE: Entered STN: 5 Mar 2005
Last Updated on STN: 6 Jul 2005
Entered Medline: 5 Jul 2005

AB In this review we focus on a promising novel histone deacetylase (HDAC) inhibitor (HA-But) obtained by the esterification of butyric acid (BA), the smallest HDAC inhibitor, with hyaluronic acid (HA), the main constituent of the extracellular matrix which selectively recognizes a transmembrane receptor (CD44) overexpressed in most primary cancers and associated with tumor progression. In vitro, HA-But has proved to be 10-fold more effective than BA in inhibiting the proliferation of a panel of human cancer cell lines, representative of the most common human cancers, and, similar to BA, to regulate the expression of some cell cycle-related proteins, to induce growth arrest in the G1/G0 phase of the cell cycle and to increase histone acetylation. In vivo, HA-But treatment has demonstrated a marked potency in inhibiting primary tumor growth and lung metastases formation from murine Lewis lung carcinoma (LL3) as well as liver metastases formation from intrasplenic implantation of LL3 or B16-F10 murine melanoma cells. In particular, the effect of s.c. and i.p. treatment with HA-But on liver metastases resulted, respectively, in 87 and 100% metastases-free animals, and in a significant prolongation of the survival time compared to the control groups. The results suggest that the presence of the HA backbone does not interfere with the biological activity of butyric residues and that HA-But could represent a promising cell-targetable antineoplastic agent for the treatment of primary and metastatic tumors.

L12 ANSWER 12 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2004364551 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15269158
TITLE: Inhibition of hepatocellular carcinomas in vitro and hepatic metastases in vivo in mice by the histone deacetylase inhibitor HA-But.
AUTHOR: Coradini Danila; Zorzet Sonia; Rossin Raffaella; Scarlata Ignazio; Pellizzaro Cinzia; Turrin Claudia; Bello Michele; Cantoni Silvia; Speranza Annalisa; Sava Gianni; Mazzi Ulderico; Perbellini Alberto
CORPORATE SOURCE: Unit of Biomolecular Determinants in Prognosis and Therapy, Experimental Department, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan.. Danila.Coradini@istitutotumori.mi.it
SOURCE: Clinical cancer research : an official journal of the American Association for Cancer Research, (2004 Jul 15) Vol. 10, No. 14, pp. 4822-30.
Journal code: 9502500. ISSN: 1078-0432.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 23 Jul 2004
Last Updated on STN: 20 Jan 2005
Entered Medline: 19 Jan 2005

AB PURPOSE: The purpose is to evaluate the CD44-mediated cellular targeting of HA-But, a hyaluronic acid esterified with

butyric acid (But) residues, to hepatocellular carcinoma cell lines in vitro and to hepatic tumor metastases in vivo. EXPERIMENTAL DESIGN: In vitro, the CD44-dependent cytotoxicity in two human hepatocellular carcinoma cell lines (HepB3 and HepG2) with high and low CD44 expression was investigated; in vivo, the effect on liver metastases originating from intrasplenic implants of Lewis lung carcinoma (LL3) or B16-F10 melanoma in mice was compared with the pharmacokinetics of organ and tissue distribution using different routes of administration. RESULTS: HepB3 and HepG2 cell lines showed different expression of CD44 (78 and 18%, respectively), which resulted in a CD44-dependent HA-But inhibitory effect as demonstrated also by the uptake analysis performed using radiolabeled HA-But ((99m)Tc-HA-But). Pharmacokinetic studies showed different rates of (99m)Tc-HA-But distribution according to the route of administration (i.v., i.p., or s.c.): very fast (a few minutes) after i.v. treatment, with substantial accumulation in the liver and spleen; relatively slow after i.p. or s.c. treatment, with marked persistence of the drug at the site of injection. The effect of s.c. and i.p. treatment with HA-But on liver metastases originating from intrasplenic implants of LL3 carcinoma or B16-F10 melanoma (both CD44-positive: 68 and 87%, respectively), resulted in 87 and 100% metastases-free animals, respectively (regardless of the route of administration), and a significant prolongation of the life expectancy compared with control groups. CONCLUSIONS: HA-But tends to concentrate in the liver and spleen and appears to be a promising new drug for the treatment of intrahepatic tumor lesions.

L12 ANSWER 13 OF 17 MEDLINE on STN

ACCESSION NUMBER: 2004222806 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15122068
TITLE: Hyaluronic-acid butyric esters as promising antineoplastic agents in human lung carcinoma: a preclinical study.
AUTHOR: Coradini Danila; Pellizzaro Cinzia; Abolafio Gabriella; Bosco Marco; Scarlata Ignazio; Cantoni Silvia; Stucchi Luca; Zorzet Sonia; Turrin Claudia; Sava Gianni; Perbellini Alberto; Daidone Maria Grazia
CORPORATE SOURCE: Unit of Biomolecular Determinants in Prognosis and Therapy, Experimental Department, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milano, Italy.. danila.coradini@istitutotumori.mi.it
SOURCE: Investigational new drugs, (2004 Aug) Vol. 22, No. 3, pp. 207-17.
Journal code: 8309330. ISSN: 0167-6997.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 5 May 2004
Last Updated on STN: 19 Dec 2004
Entered Medline: 22 Nov 2004

AB New promising compounds, derived from the esterification of hyaluronic acid with butyric acid, were investigated in vitro on a non-small cell lung carcinoma cell line (NCI-H460) and an its metastatic subclone (NCI-H460M). All new compounds exerted a dose-dependent inhibitory effect on both cell lines, which expressed CD44, the specific surface receptor for hyaluronic acid, in a very high percentage of cells (90%). HE1, the most effective of these compounds, was 10-fold more effective than sodium butyrate (NaB) in inhibiting cell proliferation. Similarly to NaB, after 24 hours of treatment, HE1 affected the expression of three cell cycle-related proteins (p27(kip1), p53 and p21(waf1)) responsible for growth arrest, indicating that the presence of the hyaluronic acid backbone does not interfere with the biologic activity. Intratumoral treatment with HE1 demonstrated a marked efficacy on primary

tumor growth and on lung metastases formation of the murine Lewis Lung Carcinoma model. Altogether, present findings suggest a possible clinical application of these novel butyric pro-drugs in primary and metastatic lung cancer.

L12 ANSWER 14 OF 17 MEDLINE on STN
ACCESSION NUMBER: 1999224662 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10209956
TITLE: Hyaluronic acid as drug delivery for sodium butyrate: improvement of the anti-proliferative activity on a breast-cancer cell line.
AUTHOR: Coradini D; Pellizzaro C; Miglierini G; Daidone M G; Perbellini A
CORPORATE SOURCE: Oncologia Sperimentale C, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy.. coradini@istitutotumori.mi.it
SOURCE: International journal of cancer. Journal international du cancer, (1999 May 5) Vol. 81, No. 3, pp. 411-6. Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 11 May 1999
Last Updated on STN: 11 May 1999
Entered Medline: 29 Apr 1999

AB The potential clinical utility of sodium butyrate, a natural compound known to inhibit tumor-cell growth, is hampered by the difficulty of achieving effective in-vivo concentrations. The short half-life (about 5 minutes) of sodium butyrate results in rapid metabolism and excretion. To increase the availability of sodium butyrate over a longer period of time, we co-valently linked it to hyaluronic acid (a component of the extracellular matrix). Its major advantages as a drug carrier consist in its high biocompatibility and its ability to bind CD44, a specific membrane receptor frequently over-expressed on the tumor-cell surface. The degree of substitution of hyaluronic acid with butyrate residues ranged from d.s.=0.10 to d.s.=2.24 (1.8-28.4% w/w). The biological activity of hyaluronic-acid-butyric-ester derivatives was evaluated in terms of the inhibition of the growth of the MCF7 cell line and compared with that of sodium butyrate. After 6 days of treatment, we observed a progressive improvement of the anti-proliferative activity up to d.s.=0.20; thereafter, the anti-proliferative effect of the ester derivatives decreased. Fluorescence microscopy showed that after 2 hr of treatment fluorescein-labelled compounds appeared to be almost completely internalized into MCF7 cells, expressing CD44 standard and variant isoforms. These findings indicate that hyaluronic acid could offer an important advantage in drug delivery, in addition to its biocompatibility: the ability to bind to CD44, which are known to be frequently over-expressed on the tumor-cell surface.

L12 ANSWER 15 OF 17 MEDLINE on STN
ACCESSION NUMBER: 97266064 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9111868
TITLE: CD44: structure, function, and association with the malignant process.
AUTHOR: Naor D; Sionov R V; Ish-Shalom D
CORPORATE SOURCE: Lautenberg Center for General and Tumor Immunology, Hebrew University-Hadassah Medical School, Jerusalem, Israel.
SOURCE: Advances in cancer research, (1997) Vol. 71, pp. 241-319. Ref: 489
Journal code: 0370416. ISSN: 0065-230X.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 9 Jul 1997
Last Updated on STN: 29 Jan 1999
Entered Medline: 20 Jun 1997

AB CD44 is a ubiquitous multistructural and multifunctional cells surface adhesion molecule involved in cell-cell and cell-matrix interactions. Twenty exons are involved in the genomic organization of this molecule. The first five and the last 5 exons are constant, whereas the 10 exons located between these regions are subjected to alternative splicing, resulting in the generation of a variable region. Differential utilization of the 10 variable region exons, as well as variations in N-glycosylation, O-glycosylation, and glycosaminoglycanation (by heparan sulfate or chondroitin sulfate), generate multiple isoforms (at least 20 are known) of different molecular sizes (85-230 kDa). The smallest CD44 molecule (85-95 kDa), which lacks the entire variable region, is standard CD44 (CD44s). As it is expressed mainly on cells of lymphohematopoietic origin, CD44s is also known as hematopoietic CD44 (CD44H). CD44s is a single-chain molecule composed of a distal extracellular domain (containing, the ligand-binding sites), a membrane-proximal region, a transmembrane-spanning domain, and a cytoplasmic tail. The molecular sequence (with the exception of the membrane-proximal region) displays high interspecies homology. After immunological activation, T lymphocytes and other leukocytes transiently upregulate CD44 isoforms expressing variant exons (designated CD44v). A CD44 isform containing the last 3 exon products of the variable region (CD44V8-10, also known as epithelial CD44 or CD44E), is preferentially expressed on epithelial cells. The longest CD44 isoform expressing in tandem eight exons of the variable region (CD44V3-10) was detected in keratinocytes. Hyaluronic acid (HA), an important component of the extracellular matrix (ECM), is the principal, but by no means the only, ligand of CD44. Other CD44 ligands include the ECM components collagen, fibronectin, laminin, and chondroitin sulfate. Mucosal addressin, serglycin, osteopontin, and the class II invariant chain (Ii) are additional, ECM-unrelated, ligands of the molecule. In many, but not in all cases, CD44 does not bind HA unless it is stimulated by phorbol esters, activated by agonistic anti-CD44 antibody, or deglycosylated (e.g., by tunicamycin). CD44 is a multifunctional receptor involved in cell-cell and cell-ECM interactions, cell traffic, lymph node homing, presentation of chemokines and growth factors to traveling cells, and transmission of growth signals. CD44 also participates in the uptake and intracellular degradation of HA, as well as in transmission of signals mediating hematopoiesis and apoptosis. Many cancer cell types as well as their metastases express high levels of CD44. Whereas some tumors, such as gliomas, exclusively express standard CD44, other neoplasms, including gastrointestinal cancer, bladder cancer, uterine cervical cancer, breast cancer and non-Hodgkin's lymphomas, also express CD44 variants. Hence CD44, particularly its variants, may be used as diagnostic or prognostic markers of at least some human malignant diseases. Furthermore, it has been shown in animal models that injection of reagents interfering with CD44-ligand interaction (e.g., CD44s- or CD44v-specific antibodies) inhibit local tumor growth and metastatic spread. These findings suggest that CD44 may confer a growth advantage on some neoplastic cells and, therefore, could be used as a target for cancer therapy. It is hoped that identification of CD44 variants expressed on cancer but not on normal cells will lead to the development of anti-CD44 reagents restricted to the neoplastic growth.

L12 ANSWER 16 OF 17 MEDLINE on STN
ACCESSION NUMBER: 93203668 MEDLINE

DOCUMENT NUMBER: PubMed ID: 8095961
TITLE: CD44 antibody stimulates adhesion of peripheral blood T cells to keratinocytes through the leukocyte function-associated antigen-1/intercellular adhesion molecule-1 pathway.
AUTHOR: Bruynzeel I; Koopman G; van der Raaij L M; Pals S T; Willemze R
CORPORATE SOURCE: Department of Dermatology, Free University Hospital, Amsterdam, The Netherlands.
SOURCE: The Journal of investigative dermatology, (1993 Apr) Vol. 100, No. 4, pp. 424-8.
Journal code: 0426720. ISSN: 0022-202X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 7 May 1993
Last Updated on STN: 3 Feb 1997
Entered Medline: 22 Apr 1993

AB Close contact between T lymphocytes and keratinocytes is an important feature of many inflammatory skin diseases. In vitro studies showed that stimulation of keratinocytes with interferon-gamma or tumor necrosis factor-alpha and of T cells with phorbol esters results in a leukocyte function-associated antigen (LFA)-1/intercellular adhesion molecule (ICAM)-1-mediated adhesion. The present study was performed to investigate the role of the CD44 molecule in keratinocyte/T-cell binding. The CD44 class of lymphocyte adhesion receptors is involved in lymphocyte binding to high endothelial venules and to extracellular matrix compounds and is therefore important in lymphocyte recirculation and homing. Moreover, CD44 can act as a co-stimulating signal in T-cell activation and promotes homotypic adhesion of in vitro cultured CD3-stimulated T cells. Using a cell adhesion assay a sixfold increase in T-cell/keratinocyte adhesion was found after pre-incubating the T cells with anti-CD44. This increased adhesion was found to require an intact cytoskeleton, to be energy and magnesium dependent, and could be completely inhibited by anti-LFA-1 and anti-ICAM-1. Pretreatment of T cells with hyaluronic acid, a ligand for CD44 and an extracellular matrix compound in the dermis and epidermis, did not affect T-cell/keratinocyte adhesion.

L12 ANSWER 17 OF 17 MEDLINE on STN
ACCESSION NUMBER: 90030452 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2805078
TITLE: Effects of thyroid-stimulating hormone and phorbol ester on glycosaminoglycan synthesis in porcine thyroid epithelial cells in primary culture.
AUTHOR: Wegrowski J; Bellon G; Haye B; Borel J P
CORPORATE SOURCE: Laboratoire de Biochimie, UA CNRS 610, Faculte de Medecine, Reims, France.
SOURCE: Cell biology international reports, (1989 Oct) Vol. 13, No. 10, pp. 881-90.
Journal code: 7708050. ISSN: 0309-1651.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198912
ENTRY DATE: Entered STN: 28 Mar 1990
Last Updated on STN: 28 Mar 1990
Entered Medline: 21 Dec 1989

AB The effects of thyroid-stimulating hormone (TSH) and a tumor promoter: 12-0-tetradecanoyl-phorbol-13-acetate on glycosaminoglycan (GAG) synthesis were studied in porcine thyroid epithelial cells in primary

culture. TSH is known to involve cyclic AMP mechanism and phorbol ester to act by protein kinase C pathway. Chronic treatment of cells with TSH increased the synthesis of heparan sulphate associated with the cell layer and hyaluronic acid in the culture medium. Phorbol ester increased the radioactivity of total GAGs in the culture medium but had no effect on GAGs associated with the cell layer. It inhibited the positive effect of TSH on heparan sulphate synthesis. These results suggest that in thyroid epithelial cells the synthesis of the GAGs associated with the cell layer and those secreted into the culture medium are regulated by different intracellular mechanisms.

L12 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:405314 CAPLUS
TITLE: HYTAD1-p20: a new paclitaxel-hyaluronic acid hydrosoluble bioconjugate for treatment of superficial bladder cancer
AUTHOR(S): Rosato, Antonio; Banzato, Alessandra; De Luca, Gilda; Renier, Davide; Bettella, Fabio; Pagano, Claudio; Esposito, Giovanni; Zanovello, Paola; Bassi, PierFrancesco
CORPORATE SOURCE: Department of Oncology and Surgical Sciences, Oncology Section, University of Padova, Padua, Italy
SOURCE: Urologic Oncology: Seminars and Original Investigations (2006), 24(3), 207-215
CODEN: UOSOAA
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This paper reports the development of a new water-soluble paclitaxel-hyaluronic acid bioconjugate, HYTAD1-p20, for intravesical treatment of superficial bladder cancer. HYTAD1-p20 was synthesized by carboxyl esterification of hyaluronic acid with paclitaxel, and its physicochem. and biol. properties were characterized. Paclitaxel loading was optimized at 20% weight/weight; this procedure increased by 500-fold the paclitaxel concentration in the resulting water-soluble biomaterial. In vitro, HYTAD1-p20 exerted a much higher dose-dependent inhibitory effect against RT-4 and RT-112/84 bladder carcinoma cell growth than that of free drug, and directly interacted with CD44 expressed by bladder tumor cells. In vivo, results of pharmacokinetic studies performed in mice after bladder catheterization and intravesical instillation of HYTAD1-p20 disclosed that drug leakage was negligible during a 2-h anal. Histol. examination of drug-instilled bladders revealed that HYTAD1-p20 was extremely well tolerated, while paclitaxel alone produced mucosal disruption and submucosal infiltration of inflammatory cells. Treatment of severe combined immunodeficient mice bearing s.c. RT-112/84 tumors with maximum tolerated doses of bioconjugate or paclitaxel showed that HYTAD1-p20 exerted a therapeutic activity comparable to that of free drug. These data suggest that HYTAD1-p20 significantly improved results obtained with conventional paclitaxel in terms of hydrosoly., in vitro activity against human bladder cancer cells, and in vivo biocompatibility. This bioconjugate is a potentially useful treatment for superficial urothelial malignancy.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:591962 CAPLUS
DOCUMENT NUMBER: 143:91004
TITLE: Use of PSP64 and subfragments to suppress cell adhesion and migration, inhibit matrix metalloproteinase secretion, and treat cancer and other diseases
INVENTOR(S): Panchal, Chandra J.; Wu, Jinzi Jason; Beliveau, Richard; Ruiz, Marcia; Garde, Seema; Annabi, Borhane; Lamy, Sylvie; Bouzeghrane, Mounia; Daigneault, Luc; Hawkins, Robert
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 59 pp., Cont.-in-part of U.S. Ser. No. 948,229.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005147601	A1	20050707	US 2004-4270	20041202
CA 2441695	AA	20050326	CA 2003-2441695	20030926
US 2005096273	A1	20050505	US 2004-948229	20040924
WO 2005118623	A1	20051215	WO 2005-CA430	20050321

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
CA 2003-2441695	A	20030926
US 2004-948229	A2	20040924
US 2004-857358	A	20040601
US 2004-4270	A	20041202
US 2004-4273	A	20041202

AB Matrix metalloproteinases (MMPs) play an important role in morphogenesis, angiogenesis, wound healing, and in certain disorders such as rheumatoid arthritis, tumor invasion and metastasis. MMPs are thought to be regulated by a variety of cytokines, growth factors, hormones and phorbol esters. This regulation occurs on three levels; alteration of gene expression, activation of the latent zymogen and inhibition by the tissue inhibitors of metalloproteinases (TIMP). We report here a new agent that regulates the level of MMPs, i.e., prostate secretory protein PSP94. Thus, PCK3145, a pentadecapeptide derived from PSP94, significantly decreased levels of MMP-9 in the blood of patients with metastatic adenocarcinoma of the prostate. A derivative of PCK3145 in which the 3 cysteine SH groups were acetaminomethylated, suppressed secretion of MMP from Mat-LyLu cells. This derivs. also decreased U-87 cell adhesion to hyaluronic acid as well as U-87 cell migration. Further effects of the PSP94 peptide derivative were increased CD44 cell surface shedding and induction of RhoA protein expression.

L12 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2005:178896 CAPLUS
DOCUMENT NUMBER:	142:384899
TITLE:	Hyaluronic acid butyric esters in cancer therapy
AUTHOR(S):	Speranza, Annalisa; Pellizzaro, Cinzia; Coradini, Danila
CORPORATE SOURCE:	Unit of Biomolecular Determinants in Prognosis and Therapy, Experimental Department, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy
SOURCE:	Anti-Cancer Drugs (2005), 16(4), 373-379 CODEN: ANTDEV; ISSN: 0959-4973
PUBLISHER:	Lippincott Williams & Wilkins
DOCUMENT TYPE:	Journal; General Review
LANGUAGE:	English

AB In this review the authors focus on a promising novel histone deacetylase (HDAC) inhibitor (HA-But) obtained by the esterification of butyric acid (BA), the smallest HDAC inhibitor, with hyaluronic acid (HA), the main constituent of the extracellular matrix which selectively recognizes a transmembrane receptor (CD44) overexpressed in most primary cancers and associated with tumor progression. In vitro, HA-But has proved to be 10-fold more

effective than BA in inhibiting the proliferation of a panel of human cancer cell lines, representative of the most common human cancers, and, similar to BA, to regulate the expression of some cell cycle-related proteins, to induce growth arrest in the G1/G0 phase of the cell cycle and to increase histone acetylation. In vivo, HA-But treatment has demonstrated a marked potency in inhibiting primary tumor growth and lung metastases formation from murine Lewis lung carcinoma (LL3) as well as liver metastases formation from intrasplenic implantation of LL3 or B16-F10 murine melanoma cells. In particular, the effect of s.c. and i.p. treatment with HA-But on liver metastases resulted, resp., in 87 and 100% metastases-free animals, and in a significant prolongation of the survival time compared to the control groups. The results suggest that the presence of the HA backbone does not interfere with the biol. activity of butyric residues and that HA-But could represent a promising cell-targetable antineoplastic agent for the treatment of primary and metastatic tumors.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:583316 CAPLUS

DOCUMENT NUMBER: 142:147954

TITLE: Inhibition of hepatocellular carcinomas in vitro and hepatic metastases in vivo in mice by the histone deacetylase inhibitor HA-But

AUTHOR(S): Coradini, Danila; Zorzet, Sonia; Rossin, Raffaella; Scarlata, Ignazio; Pellizzaro, Cinzia; Turrin, Claudia; Bello, Michele; Cantoni, Silvia; Speranza, Annalisa; Sava, Gianni; Mazzi, Ulderico; Perbellini, Alberto

CORPORATE SOURCE: Unit of Biomolecular Determinants in Prognosis and Therapy, Experimental Department, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy

SOURCE: Clinical Cancer Research (2004), 10(14), 4822-4830
CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The purpose is to evaluate the CD44-mediated cellular targeting of HA-But, a hyaluronic acid esterified with butyric acid (But) residues, to hepatocellular carcinoma cell lines in vitro and to hepatic tumor metastases in vivo. In vitro, the CD44-dependent cytotoxicity in two human hepatocellular carcinoma cell lines (HepB3 and HepG2) with high and low CD44 expression was investigated; in vivo, the effect on liver metastases originating from intrasplenic implants of Lewis lung carcinoma (LL3) or B16-F10 melanoma in mice was compared with the pharmacokinetics of organ and tissue distribution using different routes of administration. HepB3 and HepG2 cell lines showed different expression of CD44 (78 and 18%, resp.), which resulted in a CD44-dependent HA-But inhibitory effect as demonstrated also by the uptake anal. performed using radiolabeled HA-But (99mTc-HA-But). Pharmacokinetic studies showed different rates of 99mTc-HA-But distribution according to the route of administration (i.v., i.p., or s.c.): very fast (a few minutes) after i.v. treatment, with substantial accumulation in the liver and spleen; relatively slow after i.p. or s.c. treatment, with marked persistence of the drug at the site of injection. The effect of s.c. and i.p. treatment with HA-But on liver metastases originating from intrasplenic implants of LL3 carcinoma or B16-F10 melanoma (both CD44-pos.: 68 and 87%, resp.), resulted in 87 and 100% metastases-free animals, resp. (regardless of the route of administration), and a significant prolongation of the life expectancy compared with control groups. HA-But tends to concentrate in the liver and spleen and appears to be a promising new drug for the treatment of intrahepatic tumor lesions.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:359113 CAPLUS
DOCUMENT NUMBER: 142:85944
TITLE: Hyaluronic-acid butyric esters as promising antineoplastic agents in human lung carcinoma: A preclinical study
AUTHOR(S): Coradini, Danila; Pellizzaro, Cinzia; Abolafio, Gabriella; Bosco, Marco; Scarlata, Ignazio; Cantoni, Silvia; Stucchi, Luca; Zorzet, Sonia; Turrin, Claudia; Sava, Gianni; Perbellini, Alberto; Daidone, Maria Grazia
CORPORATE SOURCE: Unit of Biomolecular Determinants in Prognosis and Therapy, Experimental Department, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Neth.
SOURCE: Investigational New Drugs (2004), 22(3), 207-217
CODEN: INNDDK; ISSN: 0167-6997
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB New promising compds., derived from the esterification of hyaluronic acid with butyric acid, were investigated in vitro on a non-small cell lung carcinoma cell line (NCI-H460) and an its metastatic subclone (NCI-H460M). All new compds. exerted a dose-dependent inhibitory effect on both cell lines, which expressed CD44, the sp. surface receptor for hyaluronic acid, in a very high percentage of cells (90%). HE1, the most effective of these compds., was 10-fold more effective than sodium butyrate (NaB) in inhibiting cell proliferation. Similarly to NaB, after 24 h of treatment, HE1 affected the expression of three cell cycle-related proteins (p27kip1, p53 and p21waf1) responsible for growth arrest, indicating that the presence of the hyaluronic acid backbone does not interfere with the biol. activity. Intratumoral treatment with HE1 demonstrated a marked efficacy on primary tumor growth and on lung metastases formation of the murine Lewis Lung Carcinoma model. Altogether, present findings suggest a possible clin. application of these novel butyric pro-drugs in primary and metastatic lung cancer.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:246222 CAPLUS
DOCUMENT NUMBER: 131:110966
TITLE: Hyaluronic acid as drug delivery for sodium butyrate: improvement of the anti-proliferative activity on a breast-cancer cell line
AUTHOR(S): Coradini, Danila; Pellizzaro, Cinzia; Miglierini, Giuliana; Daidone, Maria Grazia; Perbellini, Alberto
CORPORATE SOURCE: Oncologia Sperimentale C, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, 20133, Italy
SOURCE: International Journal of Cancer (1999), 81(3), 411-416
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The potential clin. utility of sodium butyrate, a natural compound known to inhibit tumor-cell growth, is hampered by the difficulty of achieving effective in-vivo concns. The short half-life (about 5 min) of sodium butyrate results in rapid metabolism and excretion. To increase the availability of sodium butyrate over a longer period of time, we co-valently linked it to hyaluronic acid (a component of the extracellular matrix). Its major advantages as a drug carrier

consist in its high biocompatibility and its ability to bind CD44, a specific membrane receptor frequently over-expressed on the tumor -cell surface. The degree of substitution of hyaluronic acid with butyrate residues ranged from d.s. = 0.10 to d.s. = 2.24 (1.8-28.4% weight/weight). The biol. activity of hyaluronic-acid-butyric-ester derivs. was evaluated in terms of the inhibition of the growth of the MCF7 cell line and compared with that of sodium butyrate. After 6 days of treatment, we observed a progressive improvement of the anti-proliferative activity up to d.s. = 0.20; thereafter, the anti-proliferative effect of the ester derivs. decreased. Fluorescence microscopy showed that after 2 h of treatment fluorescein-labeled compds. appeared to be almost completely internalized into MCF7 cells, expressing CD44 standard and variant isoforms. These findings indicate that hyaluronic acid could offer an important advantage in drug delivery, in addition to its biocompatibility: the ability to bind to CD44, which are known to be frequently over-expressed on the tumor-cell surface.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:591962 CAPLUS
DOCUMENT NUMBER: 143:91004
TITLE: Use of PSP64 and subfragments to suppress cell adhesion and migration, inhibit matrix metalloproteinase secretion, and treat cancer and other diseases
INVENTOR(S): Panchal, Chandra J.; Wu, Jinzi Jason; Beliveau, Richard; Ruiz, Marcia; Garde, Seema; Annabi, Borhane; Lamy, Sylvie; Bouzeghrane, Mounia; Daigneault, Luc; Hawkins, Robert
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 59 pp., Cont.-in-part of U.S. Ser. No. 948,229.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005147601	A1	20050707	US 2004-4270	20041202
CA 2441695	AA	20050326	CA 2003-2441695	20030926
US 2005096273	A1	20050505	US 2004-948229	20040924
WO 2005118623	A1	20051215	WO 2005-CA430	20050321

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

CA 2003-2441695	A	20030926
US 2004-948229	A2	20040924
US 2004-857358	A	20040601
US 2004-4270	A	20041202
US 2004-4273	A	20041202

AB Matrix metalloproteinases (MMPs) play an important role in morphogenesis, angiogenesis, wound healing, and in certain disorders such as rheumatoid arthritis, tumor invasion and metastasis. MMPs are thought to be regulated by a variety of cytokines, growth factors, hormones and phorbol esters. This regulation occurs on three levels; alteration of gene expression, activation of the latent zymogen and inhibition by the tissue inhibitors of metalloproteinases (TIMP). We report here a new agent that regulates the level of MMPs, i.e., prostate secretory protein PSP94. Thus, PCK3145, a pentadecapeptide derived from PSP94, significantly decreased levels of MMP-9 in the blood of patients with metastatic adenocarcinoma of the prostate. A derivative of PCK3145 in which the 3 cysteine SH groups were acetaminomethylated, suppressed secretion of MMP from Mat-LyLu cells. This derivs. also decreased U-87 cell adhesion to hyaluronic acid as well as U-87 cell migration. Further effects of the PSP94 peptide derivative were increased CD44 cell surface shedding and induction of RhoA protein expression.

L18 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:969196 CAPLUS
DOCUMENT NUMBER: 143:278202
TITLE: Decreasing the metastatic potential in cancers - targeting the heparan sulfate proteoglycans
AUTHOR(S): Fjeldstad, K.; Kolset, S. O.
CORPORATE SOURCE: Department of Nutrition, Institute of Basic Medical Sciences, Oslo, 0316, Norway
SOURCE: Current Drug Targets (2005), 6(6), 665-682
CODEN: CDTUAU; ISSN: 1389-4501
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The heterogeneity of proteoglycans (PG)s contributes to their functional diversity. Many functions depend on their ability to bind and modulate the activity of components of the extracellular matrix (ECM). The ability of PGs to interact with other mols., such as growth factors, is largely determined by the fine structure of the glycosaminoglycan (GAG) chains. Tumorigenesis is associated with changes in the PG synthesis. Heparan sulfate (HS) PGs are involved in several aspects of cancer biol. including tumor progression, angiogenesis, and metastasis. PGs can have both tumor promoting and tumor suppressing activities depending on the protein core, the GAG attached, mols. they associate with, localization, the tumor subtype, stages, and degree of tumor differentiation. Perlecan is an angiogenic factor involved in tumor invasiveness. The C-terminal domain V of perlecan, named endorepellin, has however been shown to inhibit angiogenesis. Another angiogenic factor is endostatin, the COOH-terminal domain of the part-time PG collagen XVIII. Glypicans and syndecans may promote local cancer cell growth in some cancer tissues, but inhibit tissue invasion and metastasis in others. The GAG hyaluronan (HA) promotes cancer growth by providing a loose matrix for migrating tumor cells and mediates adhesion of cancer cells. HSPG degrading enzymes like heparanase, heparitinase, and other enzymes such as hyaluronidase and MMP are also important in tumor metastasis. Several different treatment strategies that target PGs have been developed. They have the potential to be effective in reducing tumor growth and inhibit the formation of metastases. PGs are also valuable tumor markers in several cancers.

REFERENCE COUNT: 284 THERE ARE 284 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:173455 CAPLUS
DOCUMENT NUMBER: 138:198601
TITLE: New drug recombinant CD44 protein
INVENTOR(S): Stroemblad, Staffan; Kogerman, Priit; Paell, Taavi
PATENT ASSIGNEE(S): Swed.
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003018044	A1	20030306	WO 2002-SE1531	20020826
WO 2003018044	C1	20040624		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2458565	AA	20030306	CA 2002-2458565		20020826
EP 1418931	A1	20040519	EP 2002-760977		20020826
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
CN 1561223	A	20050105	CN 2002-819275		20020826
JP 2005525995	T2	20050902	JP 2003-522561		20020826
US 2005054593	A1	20050310	US 2004-487620		20040524
PRIORITY APPLN. INFO.:			SE 2001-2823	A	20010824
			US 2001-314971P	P	20010824
			WO 2002-SE1531	W	20020826

AB CD44, the receptor for hyaluronic acid, has complex functions in cellular physiol., cell migration and tumor metastasis. The inventors have previously found that human CD44 receptor overexpression in mouse fibrosarcoma cells inhibits s.c. tumor growth in mice. Here it is demonstrated that a tumor growth inhibitory effect of CD44 is caused by block of angiogenesis. Furthermore, the inventors have found that soluble recombinant CD44 hyaluronic acid binding domain (CD44HABD) inhibits angiogenesis in vivo in cLick and mouse and thereby inhibits human tumor growth of various origins. The anti-angiogenic effect of CD44-HABD is independent of hyaluronic acid (HA) binding, since non-HA-binding mutants of CD44HABD still maintain anti-angiogenic properties. The invention discloses soluble CD44 recombinant proteins as a novel class of angiogenesis inhibitors based on targeting of vascular cell surface receptor. A method of block of angiogenesis and treatment of human tumors using recombinant CD44 proteins as well as their analogs is disclosed. As a further embodiment of the invention, methods for screening for new drug targets using CD44 recombinant proteins and their analogs is presented.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:449951 CAPLUS
DOCUMENT NUMBER: 133:348202
TITLE: Is hyaluronan degradation an angiogenic/metastatic switch?
AUTHOR(S): West, David C.; Chen, Haijuan
CORPORATE SOURCE: Departments of Immunology and Haematology, University of Liverpool, Liverpool, L69 3GA, UK
SOURCE: International Congress Series (2000), 1196(New Frontiers in Medical Sciences: Redefining Hyaluronan), 77-86
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 60 refs.is given including the authors' own works. Macromol. hyaluronan (HA) has consistently been shown to inhibit angiogenesis, in both in vivo and in vitro exptl. models. The inhibitory effects of HA appear to be dependent on its size and concentration Examination of the relationship between HA metabolism and vascularization in wound healing models has shown a close temporal coincidence between HA-degradation and the onset and rate of neovascularization. As in previous developmental studies, an increase in tissue hyaluronidase activity accompanied the degradation of tissue

HA and angiogenesis. Recent studies on transplantable tumors and cultured tumor cell lines indicate that tumor metastasis and angiogenesis are associated with increased HA degradation and elevated hyaluronidase levels. These data suggest that the onset and degree of tissue angiogenesis is dependent on the level of hyaluronidase-mediated degradation of tissue HA. At least in tumors, this appears to be due to a GPI-anchored "neutral" cell surface hyaluronidase similar to the sperm surface hyaluronidase, PH-20. RT-PCR and Northern anal. confirmed the presence of PH-20 in most tumor cell lines. The level of PH-20 expression increased with the level of angiogenesis and metastatic potential. Using substrate gel electrophoresis and PCR, a second extracellular hyaluronidase, HYAL1, was detected in some cell lines, but its significance is not yet clear.

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:25217 CAPLUS

DOCUMENT NUMBER: 130:195576

TITLE: Hyaluronan fragments synergize with interferon-γ to induce the C-X-C chemokines Mig and interferon-inducible protein-10 in mouse macrophages

AUTHOR(S): Horton, Maureen R.; McKee, Charlotte M.; Bao, Clare; Liao, Fang; Farber, Joshua M.; Hodge-DuFour, Jennifer; Pure, Ellen; Oliver, Bonnie L.; Wright, Timothy M.; Noble, Paul W.

CORPORATE SOURCE: Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, 21205, USA

SOURCE: Journal of Biological Chemistry (1998), 273(52), 35088-35094
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Hallmarks of chronic inflammation and tissue fibrosis are increased influx of activated inflammatory cells, mediator release, and increased turnover and production of the extracellular matrix (ECM). Recent evidence has suggested that fragments of the ECM component hyaluronan play a role in chronic inflammation by inducing macrophage expression of chemokines. Interferon-γ (IFN-γ), an important regulator of macrophage functions, has been shown to induce the C-X-C chemokines Mig and IP-10. These chemokines affect T-cell recruitment and inhibit angiogenesis. The purpose here was to determine the effect of hyaluronan (HA) on IFN-γ-induced Mig and IP-10 expression in mouse macrophages. The authors found a marked synergy between HA and IFN-γ on Mig and IP-10 mRNA and protein expression in mouse macrophages. This was most significant with Mig, which was not induced by HA alone. The synergy was specific for HA, was not dependent on new protein synthesis, was not mediated by tumor necrosis factor-α, was selective for Mig and IP-10, and occurred at the level of gene transcription. Thus, the ECM component HA may influence chronic inflammatory states by working in concert with IFN-γ to alter macrophage chemokine expression.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:225148 CAPLUS

DOCUMENT NUMBER: 129:1915

TITLE: Crystal structure of the angiogenesis inhibitor endostatin at 1.5 Å resolution

AUTHOR(S): Hohenester, Erhard; Sasaki, Takako; Olesen, Bjorn R.;

Timpl, Rupert
CORPORATE SOURCE: Department of Crystallography, Birkbeck College, London, WC1E 7HX, UK
SOURCE: EMBO Journal (1998), 17(6), 1656-1664
CODEN: EMJODG; ISSN: 0261-4189
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A number of extracellular proteins contain cryptic inhibitors of angiogenesis. Endostatin is a 20 kDa C-terminal proteolytic fragment of collagen XVIII that potently inhibits endothelial cell proliferation and angiogenesis. Therapy of exptl. cancer with endostatin leads to tumor dormancy and does not induce resistance. We have expressed recombinant mouse endostatin and determined its crystal structure at 1.5 Å resolution The structure reveals a compact fold distantly related to the C-type lectin carbohydrate recognition domain and the hyaluronan -binding Link module. The high affinity of endostatin for heparin is explained by the presence of an extensive basic patch formed by 11 arginine residues. Endostatin may inhibit angiogenesis by binding to the heparan sulfate proteoglycans involved in growth factor signalling.
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:612289 CAPLUS
DOCUMENT NUMBER: 103:212289
TITLE: Regulation of cell growth by vitreous humor
AUTHOR(S): Lutty, Gerald A.; Mello Robert J.; Chandler, Carol; Fait, Carolyn; Bennett, Alonzo; Patz, Arnall
CORPORATE SOURCE: Wilmer Eye Inst., Johns Hopkins Sch. Med., Baltimore, MD, 21205, USA
SOURCE: Journal of Cell Science (1985), 76, 53-65
CODEN: JNCSAI; ISSN: 0021-9533
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Exts. of normal vitreous inhibited angiogenesis in 2 animal models: tumor-induced neovascularization in the rabbit corneal micropocket and retinal extract-induced angiogenesis in the chick chorioallantoic membrane assay. Using in vitro assays, it was found recently that an extract of bovine vitreous, free of hyaluronic acid, inhibits proliferation of cells in the aortic wall, i.e., endothelium and smooth muscle cells, as well as capillary and corneal endothelium. The inhibition is dose-dependent, as determined by either cell amount or [3H]thymidine incorporation, and not due to cytotoxicity, as demonstrated with a double-label thymidine assay. The inhibitor is trypsin sensitive and heat stable (95° for 10 min). Conversely, proliferation of pericytes, lens epithelium, and fibroblasts (dermal and corneal) was stimulated by the vitreous extract This mitogenic activity was heat labile. Growth of pigment epithelium and several tumor cell lines was unaffected. Normal vitreous apparently contains a heat-stable growth inhibitor specific for endothelium and smooth muscle cells, and a nonspecific heat-labile mitogen. The paradoxical effect of this antiangiogenic factor on arterial and capillary contractile cells, smooth muscle, and pericytes, suggests a basic difference in the regulation of the 2 vasculatures. A substance in normal vitreous may be important in controlling neovascularization that results from diabetic and other retinopathies, and could be useful for inhibiting tumor -induced angiogenesis.

L18 ANSWER 7 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2005506878 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16178800
TITLE: Decreasing the metastatic potential in cancers--targeting

the heparan sulfate proteoglycans.
AUTHOR: Fjeldstad K; Kolset S O
CORPORATE SOURCE: Institute of Basic Medical Sciences, Department of Nutrition, P.O. Box 1046 Blindern, 0316 Oslo, Norway.
SOURCE: Current drug targets, (2005 Sep) Vol. 6, No. 6, pp. 665-82. Ref: 284
Journal code: 100960531. ISSN: 1389-4501.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200510
ENTRY DATE: Entered STN: 24 Sep 2005
Last Updated on STN: 15 Oct 2005
Entered Medline: 14 Oct 2005

AB The heterogeneity of proteoglycans (PG)s contributes to their functional diversity. Many functions depend on their ability to bind and modulate the activity of components of the extracellular matrix (ECM). The ability of PGs to interact with other molecules, such as growth factors, is largely determined by the fine structure of the glycosaminoglycan (GAG) chains. Tumorigenesis is associated with changes in the PG synthesis. Heparan sulfate (HS) PGs are involved in several aspects of cancer biology including tumor progression, angiogenesis, and metastasis. PGs can have both tumor promoting and tumor suppressing activities depending on the protein core, the GAG attached, molecules they associate with, localization, the tumor subtype, stages, and degree of tumor differentiation. Perlecan is an angiogenic factor involved in tumor invasiveness. The C-terminal domain V of perlecan, named endorepellin, has however been shown to inhibit angiogenesis. Another angiogenic factor is endostatin, the COOH-terminal domain of the part-time PG collagen XVIII. Glypicans and syndecans may promote local cancer cell growth in some cancer tissues, but inhibit tissue invasion and metastasis in others. The GAG hyaluronan (HA) promotes cancer growth by providing a loose matrix for migrating tumor cells and mediates adhesion of cancer cells. HSPG degrading enzymes like heparanase, heparitinase, and other enzymes such as hyaluronidase and MMP are also important in tumor metastasis. Several different treatment strategies that target PGs have been developed. They have the potential to be effective in reducing tumor growth and inhibit the formation of metastases. PGs are also valuable tumor markers in several cancers.

L18 ANSWER 8 OF 9 MEDLINE on STN
ACCESSION NUMBER: 1999074288 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9857043
TITLE: Hyaluronan fragments synergize with interferon-gamma to induce the C-X-C chemokines mig and interferon-inducible protein-10 in mouse macrophages.
AUTHOR: Horton M R; McKee C M; Bao C; Liao F; Farber J M; Hodge-DuFour J; Pure E; Oliver B L; Wright T M; Noble P W
CORPORATE SOURCE: Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205, USA.
CONTRACT NUMBER: 5F32HL09614-02 (NHLBI)
K11HL02880 (NHLBI)
R01HL60539 (NHLBI)
SOURCE: The Journal of biological chemistry, (1998 Dec 25) Vol. 273, No. 52, pp. 35088-94.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 16 Feb 1999
Last Updated on STN: 16 Feb 1999
Entered Medline: 3 Feb 1999

AB Hallmarks of chronic inflammation and tissue fibrosis are increased influx of activated inflammatory cells, mediator release, and increased turnover and production of the extracellular matrix (ECM). Recent evidence has suggested that fragments of the ECM component hyaluronan play a role in chronic inflammation by inducing macrophage expression of chemokines. Interferon-gamma (IFN-gamma), an important regulator of macrophage functions, has been shown to induce the C-X-C chemokines Mig and IP-10. These chemokines affect T-cell recruitment and inhibit angiogenesis. The purpose of this investigation was to determine the effect of hyaluronan (HA) on IFN-gamma-induced Mig and IP-10 expression in mouse macrophages. We found a marked synergy between HA and IFN-gamma on Mig and IP-10 mRNA and protein expression in mouse macrophages. This was most significant with Mig, which was not induced by HA alone. The synergy was specific for HA, was not dependent on new protein synthesis, was not mediated by tumor necrosis factor-alpha, was selective for Mig and IP-10, and occurred at the level of gene transcription. These data suggest that the ECM component HA may influence chronic inflammatory states by working in concert with IFN-gamma to alter macrophage chemokine expression.

L18 ANSWER 9 OF 9 MEDLINE on STN
ACCESSION NUMBER: 88092358 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2447383
TITLE: Fibrin containing gels induce angiogenesis. Implications for tumor stroma generation and wound healing.
AUTHOR: Dvorak H F; Harvey V S; Estrella P; Brown L F; McDonagh J; Dvorak A M
CORPORATE SOURCE: Department of Pathology, Beth Israel Hospital, Boston, Massachusetts.
CONTRACT NUMBER: CA-28741 (NCI)
CA-28834 (NCI)
CA-40624 (NCI)
SOURCE: Laboratory investigation; a journal of technical methods and pathology, (1987 Dec) Vol. 57, No. 6, pp. 673-86.
Journal code: 0376617. ISSN: 0023-6837.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198802
ENTRY DATE: Entered STN: 5 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 2 Feb 1988

AB Fibrin deposition is a consistent early event in solid tumors and healing wounds and precedes new blood vessel ingrowth in both. We now demonstrate that fibrin gels of themselves induce an angiogenic response in the absence of tumor cells or platelets. Angiogenesis was enhanced when certain chemoattractants or mitogens were included in the fibrin gel. Newly devised, inert plastic chambers with one porous surface were filled with varying contents and were implanted in the subcutaneous space of guinea pigs. Chambers filled with cross-linked homologous fibrin or plasma induced an angiogenic response within 4 days. Vessels entered chambers through the surface pores and flared out radially; angiogenesis was quantitated by point counting. Vessels were functional and matured along a gradient that proceeded from distal (least mature) to proximal. The intensity of the angiogenic response was enhanced when zymosan activated serum, an N-formylmethionine tripeptide, or platelet-derived growth factor was included in the fibrin matrix. Prior aldehyde fixation or boiling of fibrin-filled chambers inhibited angiogenesis, as did high concentrations of hyaluronic

acid. Chambers filled with type I collagen or agarose did not induce new blood vessel formation, but addition of collagen did not reduce fibrin's capacity to initiate angiogenesis. The novel assay introduced here offers several advantages that should facilitate the study of angiogenesis. These include reproducibility, low background, objective and quantitative scoring, and the capacity to evaluate native molecules in animals of several species. Taken together, our findings strongly implicate fibrin or related proteins in the pathogenesis of angiogenesis and offer a new approach for elucidating the underlying molecular mechanisms.

L20 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:551368 CAPLUS
DOCUMENT NUMBER: 139:122818
TITLE: Biomaterials based on hyaluronic acid for the anti-angiogenic therapy in the treatment of tumors
INVENTOR(S): Fusenig, Norbert E.; Stark, Hans-Juergen; Willhauck, Michael; Pavesio, Alessandra
PATENT ASSIGNEE(S): Fidia Farmaceutici S.p.A., Italy; Deutsches Krebsforschungszentrum (DKFZ)
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057203	A2	20030717	WO 2003-EP78	20030107
WO 2003057203	A3	20031231		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2472880	AA	20030717	CA 2003-2472880	20030107
AU 2003201618	A1	20030724	AU 2003-201618	20030107
EP 1463541	A2	20041006	EP 2003-700315	20030107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005524619	T2	20050818	JP 2003-557561	20030107
US 2005037049	A1	20050217	US 2004-501030	20040812

PRIORITY APPLN. INFO.:		
IT 2002-PD3	A	20020111
WO 2003-EP78	W	20030107

AB The use in the medical-surgical field of biomaterials based on hyaluronic acid derivs., optionally in association with natural, synthetic or semi-synthetic biopolymers, for suppressing the angiogenic process associated with tumor proliferation (in primary and secondary tumors) is disclosed. For example, the Hyaff 11-based biomaterial proved able to modulate/inhibit the angiogenic process related to vascularization of the cancerous epithelium.

L26 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:617437 CAPLUS
DOCUMENT NUMBER: 119:217437
TITLE: Drugs containing hyaluronic acid for the topical treatment of skin diseases.
INVENTOR(S): Falk, Rudolf Edgar; Asculai, Samuel Simon; Klein, Ehud Shmuel; Harper, David William; Hochman, David; Purschke, Don
PATENT ASSIGNEE(S): Norpharmco Inc., Can.
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 24
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9316732	A1	19930902	WO 1993-CA61	19930216
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
CA 2061703	AA	19930821	CA 1992-2061703	19920220
CA 2061703	C	20020702		
AU 9334888	A1	19930913	AU 1993-34888	19930216
EP 626863	A1	19941207	EP 1993-903754	19930216
EP 626863	B1	20010425		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07506812	T2	19950727	JP 1993-514407	19930216
IN 175918	A1	19951028	IN 1993-CA94	19930216
HU 75089	A2	19970428	HU 1993-3282	19930216
PL 173211	B1	19980227	PL 1993-301149	19930216
NZ 299280	A	20001222	NZ 1993-299280	19930216
AT 200736	E	20010515	AT 1993-903754	19930216
ES 2156124	T3	20010616	ES 1993-903754	19930216
PT 626863	T	20010830	PT 1993-903754	19930216
CZ 290637	B6	20020911	CZ 1993-230	19930218
CN 1084064	A	19940323	CN 1993-103488	19930220
CN 1103219	B	20030319		
FI 9403789	A	19941003	FI 1994-3789	19940817
FI 113522	B1	20040514		
NO 9403044	A	19941019	NO 1994-3044	19940817
NO 312939	B1	20020722		
IN 179130	A1	19970830	IN 1995-CA272	19950313
IN 182267	A1	19990227	IN 1995-CA270	19950313
IN 182348	A1	19990327	IN 1995-CA271	19950313
IN 178280	A1	19970322	IN 1995-CA293	19950314
US 6140312	A	20001031	US 1995-466714	19950606
CA 2268476	AA	19980430	CA 1996-2268476	19961018
AU 9672721	A1	19980515	AU 1996-72721	19961018
AU 739701	B2	20011018		
EP 952855	A1	19991103	EP 1996-934250	19961018
EP 952855	B1	20050727		
R: DE, FR, GB, IT, SE				
NZ 335259	A	20001222	NZ 1996-335259	19961018
ZA 9608847	A	19970527	ZA 1996-8847	19961022
US 6475795	B1	20021105	US 1997-860696	19970616
AU 9742732	A1	19980115	AU 1997-42732	19971020
HK 1005983	A1	20010817	HK 1998-105085	19980610
GR 3036164	T3	20011031	GR 2001-401015	20010702
US 2003036525	A1	20030220	US 2002-234355	20020904

PRIORITY APPLN. INFO.:

CA 1992-2061703	A	19920220
CA 1992-2061566	A	19920220
IN 1993-CA94	A1	19930216
WO 1993-CA61	A	19930216
WO 1996-CA700	A	19961018
US 1997-860696	A1	19970616

AB Compns. comprising hyaluronic acid and a nonsteroidal antiinflammatory agent or a neoplasm inhibitor are topical drugs for the treatment of skin diseases, especially cancers. A formulation comprised diclofenac sodium 45, Na hyaluronate 37.5, benzyl alc. 15, methoxypolyethylene glycol 300 g, and water to 1200 mL. The formulation was successful in the treatment of human basal cell carcinoma. Hyaluronic acid facilitates transport of the 2nd drug.

L26 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:171016 CAPLUS
DOCUMENT NUMBER: 116:171016
TITLE: Mucin synthesis and secretion in relation to spontaneous differentiation of colon cancer cells in vitro
AUTHOR(S): Niv, Yaron; Byrd, James C.; Ho, Samuel B.; Dahiya, Rajvir; Kim, Young S.
CORPORATE SOURCE: Gastrointest. Res. Lab., VA Med. Cent., San Francisco, CA, 94121, USA
SOURCE: International Journal of Cancer (1992), 50(1), 147-52
CODEN: IJCNAW; ISSN: 0020-7136
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The synthesis and secretion of mucin-like high-mol. glycoprotein was studied in 2 human colon cancer cell lines that spontaneously differentiate in culture (Caco-2 and T84) and in 2 cell lines that do not spontaneously differentiate (LS174T and HT29). Mucin, quantitated by 3H-glucosamine labeling and chromatog. on Sepharose CL-4B, was produced by all 4 cell lines. The mucinous nature of the labeled high-mol. glycoprotein was verified by enzymic degradation treatments (heparinase, hyaluronidase, chondroitinase ABC, and N-glycanase), alkaline-borohydride treatment, inhibition of labeling by the glycosylation inhibitor benzyl-α-GalNAc, and by CsCl-d.-gradient centrifugation. In all 4 cell lines, an inverse correlation of mucin synthesis with cell d. was demonstrated. In Caco-2 cells, the spontaneous post-confluent enterocytic differentiation with increased brush-border enzyme expression was associated with a decrease in mucin synthesis and in the activities of polypeptidyl GalNAc transferase and β1,3-galactosyltransferase activity. Using cDNA probes for 2 distinct human intestinal mucins (MUC2 and MUC3), all 4 colon cancer cell lines expressed mucin message, but the types of mucin mRNA expressed differed. Thus, mucin-like glycoproteins can be synthesized by cell lines derived from non-mucinous colon cancer , whether or not they undergo spontaneous differentiation in culture. These cell lines may serve as in vitro models for studying apomucin heterogeneity and control of mucin gene expression.

L26 ANSWER 3 OF 3 MEDLINE on STN
ACCESSION NUMBER: 92098199 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1728605
TITLE: Mucin synthesis and secretion in relation to spontaneous differentiation of colon cancer cells in vitro.
AUTHOR: Niv Y; Byrd J C; Ho S B; Dahiya R; Kim Y S
CORPORATE SOURCE: Gastrointestinal Research Laboratory, VA Medical Center, San Francisco, CA.
CONTRACT NUMBER: CA45967 (NCI)
SOURCE: International journal of cancer. Journal international du cancer, (1992 Jan 2) Vol. 50, No. 1, pp. 147-52.

Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199202
ENTRY DATE: Entered STN: 23 Feb 1992
Last Updated on STN: 3 Feb 1997
Entered Medline: 4 Feb 1992

AB The synthesis and secretion of mucin-like high-molecular glycoprotein was studied in 2 human colon cancer cell lines that spontaneously differentiate in culture (Caco-2 and T84) and in 2 cell lines that do not spontaneously differentiate (LS174T and HT29). Mucin, quantitated by 3H-glucosamine labelling and chromatography on Sepharose CL-4B was found to be produced by all 4 cell lines. The mucinous nature of the labelled high-molecular glycoprotein was verified by enzymatic degradation treatments (heparinase, hyaluronidase, chondroitinase ABC, and N-glycanase), alkaline-borohydride treatment, inhibition of labelling by the glycosylation inhibitor benzyl -alpha-GalNAc, and by CsCl-density-gradient centrifugation. In all 4 cell lines, an inverse correlation of mucin synthesis with cell density was demonstrated. In Caco-2 cells, the spontaneous post-confluent enterocytic differentiation with increased brush-border enzyme expression was associated with a decrease in mucin synthesis and in the activities of polypeptidyl GalNAc transferase and beta 1,3-galactosyltransferase activity. Using cDNA probes for 2 distinct human intestinal mucins (MUC2 and MUC3), we found that all 4 colon cancer cell lines expressed mucin message, but the types of mucin mRNA expressed differed. These data indicate that mucin-like glycoproteins can be synthesized by cell lines derived from non-mucinous colon cancer, whether or not they undergo spontaneous differentiation in culture. These cell lines may serve as in vitro models for studying apomucin heterogeneity and control of mucin gene expression.

L28 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:142259 CAPLUS
DOCUMENT NUMBER: 104:142259
TITLE: Mucopolysaccharides as neoplasm inhibitors
INVENTOR(S): Sakurai, Katsukiyo; Horie, Katsuyuki; Sakamoto, Takashi; Okuyama, Takashi
PATENT ASSIGNEE(S): Seikagaku Kogyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61000017	A2	19860106	JP 1984-118283	19840611
JP 04056805	B4	19920909		
PRIORITY APPLN. INFO.:			JP 1984-118283	19840611

AB Hyaluronic acid, crosslinked hyaluronic acid, and its salts are neoplasm inhibitors. Thus, hyaluronic acid (0.25 mg/mouse/day) in saline injected i.p. into mice bearing mammary gland tumor cells in blood prevented the metastasis of the tumor.

L28 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:248089 CAPLUS
DOCUMENT NUMBER: 142:443764
TITLE: The TSG-6 and IαI Interaction Promotes a Transesterification Cleaving the Protein-Glycosaminoglycan-Protein (PGP) Cross-link
AUTHOR(S): Sanggaard, Kristian W.; Karring, Henrik; Valnickova, Zuzana; Thogersen, Ida B.; Enghild, Jan J.
CORPORATE SOURCE: Center for Insoluble Protein Structure, Department of Molecular Biology, University of Aarhus, Aarhus C, DK-8000, Den.
SOURCE: Journal of Biological Chemistry (2005), 280(12), 11936-11942
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB During co-incubation of human inter-α- inhibitor (IαI) and human tumor necrosis factor-stimulated gene 6 protein (TSG-6) SDS-stable interactions are formed between the two proteins. We have analyzed the products of this reaction and characterized the mechanism of complex formation. Following the incubation seven new bands not previously identified were apparent in SDS-PAGE. Three of these bands did not contain TSG-6, including heavy chain (HC)1·bikunin, HC2·bikunin, and free bikunin. In addition high mol. weight complexes composed of the same components as IαI, including HC1, HC2, and bikunin, were formed. The formation of these complexes was prevented by the addition of hyaluronan. The crosslinks stabilizing these complexes display properties similar to the protein-glycosaminoglycan-protein (PGP) crosslink. The TSG-6-containing SDS-stable complexes were composed of HC1·TSG-6 or HC2·TSG-6 exclusively. Both glycosylated and non-glycosylated TSG-6 participated in the complex formation. The HC·TSG-6 crosslinks were different from the PGP crosslink and were determined to be ester bonds between the α-carbonyl of the C-terminal Asp of the heavy chain and most likely a hydroxyl group containing the TSG-6 residue. The mechanism involved cleaving the PGP crosslink of IαI during a transesterification reaction. A TSG-6 hydroxyl group reacts with the ester bond between the α-carbonyl of the C-terminal Asp residues of HC1 or HC2 and carbon-6 of an internal N-acetylgalactosamine of the chondroitin-4-sulfate chain. An intermediate is formed resulting in a partitioning of the reaction between HC(1 or 2)·TSG-6 complexes and transfer of HC(1 or 2) to the chondroitin via competing pathways.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:9656 CAPLUS
DOCUMENT NUMBER: 139:169212
TITLE: Cell attachment and growth on solid hyaluronan (hylan B gel)
AUTHOR(S): Balazs, Endre A.; Eliezer-Pye, Ilana K.; Dennebaum, Rita A.; Larsen, Nancy E.; Whetstone, Julie L.
CORPORATE SOURCE: Biomatrix, Inc., Ridgefield, NJ, 07657, USA
SOURCE: Hyaluronan, [Proceedings of the International Cellucon Conference], 12th, Wrexham, United Kingdom, 2000 (2002), Meeting Date 2000, Volume 2, 33-38. Editor(s): Kennedy, John F. Woodhead Publishing Ltd.: Cambridge, UK.
CODEN: 69DKVZ; ISBN: 1-85573-570-9
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Hylan B is a water-insol. hyaluronan produced by bis-Et sulfone covalent crosslinks. Hylan B gels containing 0.5% hyaluronan polymers are heat stable, but degradable by various hyaluronidase. They are more resistant to degradation by free radicals than high mol. weight (average MW > 4 million) hyaluronan of hylan A (avg. MW 6 million). Cells after trypsin treatment were seeded on the surface of hylan B gels imbibed with tissue culture media supplemented with fetal bovine serum. Cells from eight established cell lines originating from fibroblasts, epithelial or endothelial cells, chondrocytes, tumor cells and stem cells were used. All but the endothelial-origin cells attach to the gel, but only the L929 fibroblasts and stem cells multiplied. Fibronectins (plasma or cellular) added to the media-imbibed gel promoted the spread of the cells of some of these cell lines, while sulfated glycosaminoglycans inhibited the spread and growth of some of these cells. Some poly-L-lysines, on the other hand, promoted their growth. First explant chicken embryonic cells were also cultured on hylan B gels. Embryonic fibroblasts from the heart migrated and multiplied on the gel surface when homologous embryo extract was added to the culture medium. The results form these in vitro cell culture studies suggest that hylan B gel matrixes may be modified by the addition of various types of cell attachment mols. as a means to promote cell attachment and growth.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:471288 CAPLUS

DOCUMENT NUMBER: 135:178485

TITLE: TSG-6 is concentrated in the extracellular matrix of mouse cumulus oocyte complexes through hyaluronan and inter-alpha-inhibitor binding

AUTHOR(S): Carrette, Odile; Nemade, Rashmi V.; Day, Anthony J.; Brickner, Amanda; Larsen, William J.

CORPORATE SOURCE: Department of Cell Biology, Neurobiology and Anatomy, Vontz Center for Molecular Studies, University of Cincinnati, Cincinnati, OH, 45267-0521, USA

SOURCE: Biology of Reproduction (2001), 65(1), 301-308
CODEN: BIREBV; ISSN: 0006-3363

PUBLISHER: Society for the Study of Reproduction

DOCUMENT TYPE: Journal

LANGUAGE: English

AB During development of ovarian follicles in mammals, cumulus cells and the oocyte form a mucoelastic mass that detaches itself from peripheral granulosa cell layers upon an ovulatory surge. The integrity of this cumulus-oocyte complex (COC) relies on the cohesiveness of a hyaluronan (HA)-enriched extracellular matrix (ECM). We previously identified a serum glycoprotein, inter-alpha-inhibitor (IαI), that is critical in organizing and stabilizing this matrix. Following an ovulatory stimulus, IαI diffuses into the follicular fluid and becomes integrated in the ECM through its association with HA. TSG-6 (the secreted product of the tumor necrosis factor-stimulated gene 6), another HA binding protein, forms a complex with IαI in synovial fluid. The purpose of this study was to investigate whether TSG-6 is involved in the ECM organization of COCs. Immunolocalization of TSG-6 and IαI in mouse COCs at different ovulatory stages was analyzed by immunofluorescence and laser confocal microscopy. IαI, TSG-6, and HA colocalized in the cumulus ECM. Western blot analyses were consistent with the presence of both TSG-6 and TSG-6/IαI complexes in ovulated COCs. These results suggest that TSG-6 has a structural role in COC matrix formation possibly mediating crosslinking of sep. HA mols. through its binding to IαI.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:477290 CAPLUS
DOCUMENT NUMBER: 131:256281
TITLE: Requirements for signal delivery through CD44: analysis using CD44-Fas chimeric proteins
AUTHOR(S): Ishiwatari-Hayasaka, Haruko; Fujimoto, Takashi; Osawa, Tomoko; Hirama, Toshiyasu; Toyama-Sorimachi, Noriko; Miyasaka, Masayuki
CORPORATE SOURCE: Department of Bioregulation, Biomedical Research Center, Osaka University Graduate School of Medicine, Suita, 565-0871, Japan
SOURCE: Journal of Immunology (1999), 163(3), 1258-1264
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CD44 is a transmembrane glycoprotein involved in various cell adhesion events, including lymphocyte migration, early hemopoiesis, and tumor metastasis. To examine the requirements of CD44 for signal delivery through the extracellular domain, we constructed a chimeric CD44 protein fused to the intracellular domain of Fas on its C-terminus. In cells expressing the CD44-Fas fusion protein, apoptosis could be induced by treatment with certain anti-CD44 mAbs alone, especially those recognizing the epitope group d, which has been previously shown to play a role in ligand binding, indicating that ligation of a specific region of the CD44 extracellular domain results in signal delivery. Of note was that appropriate ligation of the epitope h also resulted in the generation of apoptotic signal, although this region was not thought to be involved in ligand binding. In contrast, the so-called blocking anti-CD44 mAbs (epitope group f) that can abrogate the binding of hyaluronate (HA) failed to induce apoptosis even after further crosslinking with the secondary Ab, indicating that a mere mAb-induced oligomerization of the chimeric proteins is insufficient for signal generation. However, these blocking mAbs were instead capable of inhibiting apoptosis induced by nonblocking mAb (epitope group h). Furthermore, a chimeric protein bearing a mutation in the HA binding domain and hence lacking the ability to recognize HA was incapable of mediating the mAb-induced apoptosis, suggesting that the functional integrity of the HA binding domain is crucial to the signal generation in CD44.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:736965 CAPLUS
DOCUMENT NUMBER: 130:93889
TITLE: Activation of human orbital fibroblasts through CD40 engagement results in a dramatic induction of hyaluronan synthesis and prostaglandin endoperoxide H synthase-2 expression. Insights into potential pathogenic mechanisms of thyroid-associated ophthalmopathy
AUTHOR(S): Cao, H. James; Wang, Hwai-Shi; Zhang, Ying; Lin, Hung-Yun; Phipps, Richard P.; Smith, Terry J.
CORPORATE SOURCE: Division of Molecular and Cellular Medicine, Department of Medicine, Albany Medical College and the Samuel S. Stratton Veterans Affairs Medical Center, Albany, NY, 12208, USA
SOURCE: Journal of Biological Chemistry (1998), 273(45), 29615-29625
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human orbital fibroblasts play a putative role in the pathogenesis of thyroid-associated ophthalmopathy (TAO). The authors hypothesize that the hyaluronan accumulation and inflammation in TAO derive from enhanced biosynthetic activities of orbital fibroblasts. CD40, a member of the tumor necrosis factor-α receptor superfamily, is a critical signaling mol. expressed by B lymphocytes. Engagement of CD40 with CD154 or CD40 ligand results in the activation of target genes. Orbital fibroblasts also display CD40. Here the authors report that CD40 engagement leads to substantial increases in hyaluronan synthesis in orbital fibroblasts. The increase is approx. 5-fold above control values, is comparable to the induction elicited by IL-1β and could be attenuated with dexamethasone but not by SC 58125, a prostaglandin endoperoxide H synthase-2 (PGHS-2)-selective inhibitor. PGHS-2 is also induced by CD40 engagement in a time-dependent manner, and this is mediated through increases in levels of steady-state mRNA. The induction of PGHS-2 leads to a dramatically enhanced prostaglandin E2 production that can be blocked by SC 58125 and dexamethasone. CD40 ligand up-regulates the synthesis of IL-1α, and blocking this cytokine with exogenous IL-1 receptor antagonist (IL-1ra) or with IL-1α neutralizing antibodies partially attenuates the induction of PGHS-2. In contrast, CD40 ligand up-regulation of hyaluronan synthesis is unaffected by IL-1ra. CD40 crosslinking enhances mitogen-activated protein kinase activation, and interrupting this pathway attenuates the PGHS-2 induction. Thus the CD40/CD40 ligand bridge represents a potentially important activational pathway for orbital fibroblasts that may underlie the cross-talk between these cells and leukocytes. These findings may be relevant to the pathogenesis of TAO and provide insights into previously unrecognized, potential therapeutic targets.

REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:895402 CAPLUS

DOCUMENT NUMBER: 123:283157

TITLE: Involvement of CD44 variant isoforms in hyaluronate adhesion by human activated T cells

AUTHOR(S): Galluzzo, Edi; Albi, Nicola; Fiorucci, Stefano; Merigiola, Carla; Ruggeri, Loredana; Tosti, Antonella; Grossi, Carlo E.; Velardi, Andrea

CORPORATE SOURCE: Dep. Clinical Medicine, Pathology and Pharmacology, Univ. Perugia, Perugia, Italy

SOURCE: European Journal of Immunology (1995), 25(10), 2932-9
CODEN: EJIMAF; ISSN: 0014-2980

PUBLISHER: VCH

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The standard, 85-94-kDa form of the hyaluronic acid (HA) receptor CD44 and a number of CD44 mRNA splice variants play important roles in immune responses and tumor metastasis. Variants carrying exon 6 (v6), or 9 (v9) products are transiently expressed on activated human T cells. Here, modulation expts. with specific monoclonal antibodies (mAb) indicate that v6 and v9 are expressed independently on distinct sets of CD44 mols., and that their combined expression is necessary for HA adhesion. Moreover, the finding that mAb-mediated crosslinking of v6 and v9 promoted cytosolic free Ca2+ mobilization and co-stimulated CD3-triggered T cell proliferation indicates that v6 and v9 possess signaling and effector function activation ability. Finally, HA-mediated signaling appears to be required for variant-dependent adhesion to HA. The observation that soluble HA promoted cytosolic free Ca2+ mobilization indicates that HA-induced Ca2+ mobilization can occur during T cell-HA interaction. Since Ca2+ mobilization was inhibited by pretreatment of cells with an anti-CD44 mAb directed against the

HA-binding domain of CD44, CD44 receptors appear to be involved in HA-mediated signal transduction. The requirement of cytosolic free Ca2+ for adhesion is shown by the fact that ionomycin (a Ca2+ ionophore) stimulated, and EGTA (a Ca2+ chelator), inhibited HA adhesion. In addition, cytoskeletal activation is required for cell adhesion to HA, since drugs that block actin polymerization, such as cytochalasin B, or actomyosin contraction, such as the calmodulin antagonist W-7, inhibited cell adhesion to HA. As this adhesion is also ADP ribosylation-sensitive, it may involve a GTP-dependent function of CD44v, i.e. ankyrin binding. Thus, there is a functional hierarchy among the CD44 mols. expressed on human peripheral blood T cells and the splice variants, as compared to the standard form, exhibit a greater HA binding ability which involves CD44-mediated signaling and effector function activation.

L28 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:685124 CAPLUS
DOCUMENT NUMBER: 123:109739
TITLE: Monoclonal antibodies to CD44 and their influence on hyaluronan recognition
AUTHOR(S): Zheng, Zhong; Katoh, Shigeki; He, Qi; Oritani, Kenji; Miyake, Kensuke; Lesley, Jayne; Hyman, Robert; Hamik, Anne; Parkhouse, R. Michael E.; et al.
CORPORATE SOURCE: Dep. of Structural Biology, Univ. of Washington, Seattle, WA, 98195, USA
SOURCE: Journal of Cell Biology (1995), 130(2), 485-95
CODEN: JCLBA3; ISSN: 0021-9525
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Antibodies to CD44 have been used to inhibit a variety of processes which include lymphohemopoiesis, lymphocyte migration, and tumor metastasis. Some, but not all, CD44-mediated functions derive from its ability to serve as a receptor for hyaluronan (HA). However, sites on CD44 that interact with either ligands or antibodies are poorly understood. Interspecies rat/mouse CD44 chimeras were used to analyze the specificity of 25 mAbs and to determine that they recognize at least seven epitopes. Amino acid substitutions that resulted in loss of antibody recognition were all located in the region of homol. to other cartilage link family proteins. While at least five epitopes were eliminated by single amino acid replacements, multiple residues had to be changed to destroy binding by other antibodies. One antibody was sensitive to changes in any of three sep. parts of the mol. and some antibodies to distinct epitopes cross-blocked each other. Certain antibodies had the ability to increase HA binding by lymphocytes but this did not correlate absolutely with antibody specificity and was only partially attributable to CD44 crosslinking. Antibodies that consistently blocked HA recognition were all sensitive to amino acid changes within a short stretch of CD44. Such blocking antibodies interacted with CD44 more strongly than ligand in competition expts. One large group of antibodies blocked ligand binding, but only with a particular cell line. This detailed anal. adds to the understanding of fundamental domains within CD44 and requirements for antibodies to influence recognition of one ligand.

L28 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:142259 CAPLUS
DOCUMENT NUMBER: 104:142259
TITLE: Mucopolysaccharides as neoplasm inhibitors
INVENTOR(S): Sakurai, Katsukiyo; Horie, Katsuyuki; Sakamoto, Takashi; Okuyama, Takashi
PATENT ASSIGNEE(S): Seikagaku Kogyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61000017	A2	19860106	JP 1984-118283	19840611
JP 04056805	B4	19920909		
PRIORITY APPLN. INFO.:			JP 1984-118283	19840611

AB Hyaluronic acid, crosslinked hyaluronic acid, and its salts are neoplasm inhibitors. Thus, hyaluronic acid (0.25 mg/mouse/day) in saline injected i.p. into mice bearing mammary gland tumor cells in blood prevented the metastasis of the tumor.

L28 ANSWER 9 OF 9 MEDLINE on STN
ACCESSION NUMBER: 1999186635 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10088774
TITLE: Synovial fluid transforming growth factor beta inhibits dendritic cell-T lymphocyte interactions in patients with chronic arthritis.
AUTHOR: Summers K L; O'Donnell J L; Heiser A; Highton J; Hart D N
CORPORATE SOURCE: Christchurch Hospital, New Zealand.
SOURCE: Arthritis and rheumatism, (1999 Mar) Vol. 42, No. 3, pp. 507-18.
Journal code: 0370605. ISSN: 0004-3591.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 20 Apr 1999
Last Updated on STN: 20 Apr 1999
Entered Medline: 5 Apr 1999

AB OBJECTIVE: To examine whether rheumatoid synovial fluid (SF) inhibits dendritic cell (DC) expression of the CD80 and CD86 costimulator molecules and contributes to SF T lymphocyte hyporesponsiveness. METHODS: Cell-free rheumatoid SF was tested for its effect on DC-stimulated autologous/allogeneic mixed lymphocyte reactions and for its effect on DC surface antigen expression, as assessed by flow cytometry. Blocking monoclonal antibodies were used to identify the SF cytokines that inhibited DC-T lymphocyte interactions. RESULTS: Low concentrations of SF (2.5%) could inhibit DC-mediated autologous and allogeneic T lymphocyte proliferation. This inhibitory effect could be reversed by neutralizing transforming growth factor beta (TGFbeta) and interleukin-2 (IL-2), but not by IL-12, in the SF. Hyaluronic acid, IL-6, IL-10, and tumor necrosis factor alpha were not associated with SF inhibition. In vitro culture alone and crosslinking with the CD40 ligand up-regulated DC CD80/CD86 expression and costimulator function, and this was not affected by inclusion of SF. In the presence of SF, DC clustered with autologous T lymphocytes showed decreased CD80 and CD86 expression, and variable CD80/CD86 decreases were observed on DC clustered with allogeneic T lymphocytes. CONCLUSIONS: TGFbeta in SF appears to suppress T lymphocyte function, which may affect both signaling to DC and the induction of DC costimulator function.

L30 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:891265 CAPLUS
DOCUMENT NUMBER: 136:25150
TITLE: Laminated wound dressing containing ascorbic acid phosphates
INVENTOR(S): Komazawa, Takao
PATENT ASSIGNEE(S): Toyobo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001340375	A2	20011211	JP 2000-162275	20000531
PRIORITY APPLN. INFO.:			JP 2000-162275	20000531

AB The wound dressing comprises (a) a nonwoven fabric, (b) polyurethane film layer having openings, and (c) a sponge layer containing hyaluronic acid and alginic acid, both of which are crosslinked with epoxy compds., and ≥1 of these 3 layers contains ascorbic acid phosphates as promoters for collagen production A polyester/rayon nonwoven fabric having thereon Pelprene (thermoplastic polyester elastomer) by spun-bond method was laminated with a polytetramethylene glycol-4,4'-dicyclohexylmethanediisocyanate-isophoronediamine copolymer film having 3-mm slits, and the laminate was placed on an aqueous solution containing noncrosslinked hyaluronic acid, hyaluronic acid crosslinked with ethylene glycol diglycidyl ether, alginic acid crosslinked with ethylene glycol diglycidyl ether, L-ascorbic acid phosphate Mg salt, and sulfadiazine Ag (antibacterial) and freeze-dried to give a wound dressing having a sponge layer, which promoted wound healing in rats.

L30 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:573126 CAPLUS
DOCUMENT NUMBER: 135:127280
TITLE: Materials for covering skin injuries
INVENTOR(S): Komazawa, Takao; Kamatani, Hiroyoshi
PATENT ASSIGNEE(S): Toyobo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001212226	A2	20010807	JP 2000-27820	20000204
PRIORITY APPLN. INFO.:			JP 2000-27820	20000204

AB An wound-covering material is prepared by laminating layers in the following order; a polyurethane film, an adhesive layer containing (meth)acrylate alkyl ester polymer, and a sponge layer containing hyaluronic acid crosslinked by epoxy compds. The laminated material may contain an antimicrobial agent. It covers wound, keeping adequate amount of moisture, and promoting wound healing. The covering may be changed with new one without causing pain in the patient and disturbing the regenerating skin tissues.

L30 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:569418 CAPLUS

DOCUMENT NUMBER: 135:157718
TITLE: Wound dressings containing epoxy-crosslinked hyaluronic acid and alginic acid
INVENTOR(S): Komazawa, Takao; Kamatani, Hiroyoshi
PATENT ASSIGNEE(S): Toyobo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001212225	A2	20010807	JP 2000-27817	20000204

PRIORITY APPLN. INFO.: JP 2000-27817 20000204

AB Wound dressings have a nonwoven fabric layer, a polyurethane film layer, and a sponge layer containing hyaluronic acid and alginic acid, both of which are crosslinked with epoxy compds. A wound dressing comprising a polyester-rayon nonwoven fabric layer,, a polytetramethylene glycol-4,4'-dicyclohexylmethane diisocyanate-isophoronediamine copolymer film layer, and a sponge layer containing hyaluronic acid crosslinked with ethylene glycol diglycidyl ether, Na alginate crosslinked with ethylene glycol diglycidyl ether, and sulfadiazine Ag (antibacterial) promoted wound healing in rabbits.

L30 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:569417 CAPLUS
DOCUMENT NUMBER: 135:157717
TITLE: Wound dressings containing epoxy-crosslinked hyaluronic acid
INVENTOR(S): Komazawa, Takao; Kamatani, Hiroyoshi
PATENT ASSIGNEE(S): Toyobo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001212222	A2	20010807	JP 2000-27818	20000204

PRIORITY APPLN. INFO.: JP 2000-27818 20000204

AB Wound dressings have a polyurethane film layer, an adhesive layer of (meth)acrylate ester polymers, a nonwoven fabric layer, and a sponge layer containing hyaluronic acid crosslinked with epoxy compds. A wound dressing comprising a polytetramethylene glycol-4,4'-dicyclohexylmethane diisocyanate-isophoronediamine copolymer film layer, an acrylic acid-vinylpyrrolidone-isooctyl acrylate copolymer adhesive layer, a polyester-rayon nonwoven fabric layer, and a sponge layer containing hyaluronic acid crosslinked with ethylene glycol diglycidyl ether and sulfadiazine Ag (antibacterial) promoted wound healing in rabbits.

L30 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:568214 CAPLUS
DOCUMENT NUMBER: 135:157715
TITLE: Wound dressings containing epoxy-crosslinked hyaluronic acid and alginic acid
INVENTOR(S): Komazawa, Takao; Kamatani, Hiroyoshi
PATENT ASSIGNEE(S): Toyobo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.

CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001212224	A2	20010807	JP 2000-27821	20000204

PRIORITY APPLN. INFO.: JP 2000-27821 20000204

AB Wound dressings have a polyurethane film layer, an adhesive layer of (meth)acrylate alkyl ester polymers, and a sponge layer containing hyaluronic acid and alginic acid, both of which are crosslinked with epoxy compds. A wound dressing comprising a polytetramethylene glycol-4,4'-dicyclohexylmethane diisocyanate-isophoronediamine copolymer film layer, an acrylic acid-vinylpyrrolidone-isooctyl acrylate copolymer adhesive layer, and a sponge layer containing hyaluronic acid crosslinked with ethylene glycol diglycidyl ether, Na alginate crosslinked with ethylene glycol diglycidyl ether, and sulfadiazine Ag (antibacterial) promoted wound healing in rabbits.

L30 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:568213 CAPLUS
DOCUMENT NUMBER: 135:157714
TITLE: Wound dressings containing epoxy-crosslinked hyaluronic acid and alginic acid
INVENTOR(S): Komazawa, Takao; Kamatani, Hiroyoshi
PATENT ASSIGNEE(S): Toyobo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001212223	A2	20010807	JP 2000-27819	20000204

PRIORITY APPLN. INFO.: JP 2000-27819 20000204

AB Wound dressings have a polyurethane film layer, an adhesive layer of (meth)acrylate alkyl ester polymers, a nonwoven fabric layer, and a sponge layer containing hyaluronic acid and alginic acid, both of which are crosslinked with epoxy compds. A wound dressing comprising a polytetramethylene glycol-4,4'-dicyclohexylmethane diisocyanate-isophoronediamine copolymer film layer, an acrylic acid-vinylpyrrolidone-isooctyl acrylate copolymer adhesive layer, a polyester-rayon nonwoven fabric layer, and a sponge layer containing hyaluronic acid crosslinked with ethylene glycol diglycidyl ether, Na alginate crosslinked with ethylene glycol diglycidyl ether, and sulfadiazine Ag (antibacterial) promoted wound healing in rabbits.

L30 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:113485 CAPLUS
DOCUMENT NUMBER: 124:156129
TITLE: Dressings for wound healing
INVENTOR(S): Kuroyanagi, Takamitsu; Tsunoda, Masaru
PATENT ASSIGNEE(S): Mitsubishi Kagaku KK, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07313585	A2	19951205	JP 1994-109804	19940524

PRIORITY APPLN. INFO.: JP 1994-109804 19940524

AB Dressings for wound healing are prepared by laminating a water-absorbing fabric with a porous polyurethane film and then laminating with a epoxy compound-crosslinked hyaluronate sponge on the polyurethane film surface. Antithrombotics such as argatroban can be incorporated into the sponge layer to prevent blood clot formation in the interface of the wound and dressing and, thus, to facilitate wound healing. The dressings were soft and bacteria-resistant, showed biocompatibility, and prevented the water vapor evaporation

L30 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:406740 CAPLUS
DOCUMENT NUMBER: 113:6740
TITLE: Preparation of crosslinked carboxy polysaccharides as biodegradable plastic materials for cosmetics and pharmaceuticals
INVENTOR(S): Della Valle, Francesco; Romeo, Aurelio
PATENT ASSIGNEE(S): Fidia S.p.A., Italy
SOURCE: Eur. Pat. Appl., 37 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 341745	A1	19891115	EP 1989-108630	19890512
EP 341745	B1	19941214		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
WO 8910941	A1	19891116	WO 1989-EP519	19890512
W: AU, DK, FI, HU, JP, KR				
AU 8935747	A1	19891129	AU 1989-35747	19890512
AU 631125	B2	19921119		
HU 53666	A2	19901128	HU 1989-3636	19890512
HU 210926	B	19950928		
JP 02504163	T2	19901129	JP 1989-505458	19890512
JP 2941324	B2	19990825		
EP 614914	A2	19940914	EP 1994-108633	19890512
EP 614914	A3	19941228		
EP 614914	B1	20000816		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ES 2064378	T3	19950201	ES 1989-108630	19890512
IL 90274	A1	19960912	IL 1989-90274	19890512
CA 1339122	A1	19970729	CA 1989-599557	19890512
JP 10324701	A2	19981208	JP 1998-152832	19890512
AT 195534	E	20000915	AT 1994-108633	19890512
ES 2151910	T3	20010116	ES 1994-108633	19890512
DK 9000109	A	19900312	DK 1990-109	19900112
DK 175386	B1	20040920		
FI 107050	B1	20010531	FI 1990-188	19900112
US 5676964	A	19971014	US 1995-465055	19950605
GR 3034651	T3	20010131	GR 2000-402339	20001023

PRIORITY APPLN. INFO.:

IT 1988-47964	A	19880513
EP 1989-108630	A3	19890512
JP 1989-505458	A3	19890512
US 1989-350919	B1	19890512
WO 1989-EP519	A	19890512

US 1993-70505 A1 19930601

AB Inter- and/or intramol. esters of acid polysaccharides containing carboxy functions (e.g. auto-crosslinked polysaccharides), wherein (1) a first portion or all of the carboxy groups are esterified with hydroxy groups of the same mol. and/or of different mols. of the acid polysaccharide and/or (2) a second portion of the carboxy groups are esterified with a mono- or polyvalent alcs. including various drugs (e.g. alkaloids, anesthetic, analgesic, antiinflammatory, antiviral, antibacterial, etc.) and optionally salified with an alkali or alkaline earth metal, Mg, Al, or an amine including various drugs (e.g. alkaloids, peptides, antipsychotics, phenothiazine, vasoconstrictors, etc.), are prepared by treating an acidic polysaccharide (e.g., hyaluronic acid, alginic acid, CM-cellulose, carboxymethylchitin) with an activating agent (e.g. 2-chloro-1-methylpyridinium iodide) and subjecting the resulting intermediate activated polysaccharide derivs. to heat or irradiation These auto-crosslinked polysaccharide acids are useful in the field of biodegradable plastic materials to manufacture sanitary and surgical articles (e.g. surgical suture thread, film for artificial skin, and sponges for the medication of wounds and lesions), for pharmaceutical vehicles for controlled-release of drugs (capsules for the s.c. implantation of medicaments or microcapsules for s.c., i.m., or i.v. injection), etc.

L30 ANSWER 16 OF 16 MEDLINE on STN

ACCESSION NUMBER: 2006704636 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 17143757
TITLE: A novel hydrogel crosslinked hyaluronan with glycol chitosan.
AUTHOR: Wang Wei
CORPORATE SOURCE: Mentor Biopolymers Ltd Herriot Watt Research Park, Edinburgh, EH14 4AP, United Kingdom,. wwang@miswaco.com
SOURCE: Journal of materials science. Materials in medicine, (2006 Dec) Vol. 17, No. 12, pp. 1259-65.
Journal code: 9013087. ISSN: 0957-4530.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 5 Dec 2006
Last Updated on STN: 5 Dec 2006

AB A novel hydrogel was prepared by crosslinking hyaluronan with glycol chitosan in aqueous solution using water soluble carbodiimide at nearly neutral pH and room temperature. The products can be easily formulated into injectable gels, various films, membranes and sponges for soft tissue augmentation, viscosupplementation, drug delivery, preventing adhesion of post operation, wound dressing and tissue engineering scaffolds. The said hydrogel has high water adsorption property and biostability. Rheololgical results of the gel showed a soft and viscoelastic structure. FTIR further confirmed the formation of amide bonds between carboxyl groups of hyaluronan and amine groups of glycol chitosan and no N-acylurea and other derivatives were identified.

L30 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:1261357 CAPLUS
TITLE: A novel hydrogel crosslinked hyaluronan with glycol chitosan
AUTHOR(S): Wang, Wei
CORPORATE SOURCE: Mentor Biopolymers Ltd Herriot Watt Research Park, Edinburgh, EH14 4AP, UK
SOURCE: Journal of Materials Science: Materials in Medicine (2006), 17(12), 1259-1265
CODEN: JSMMEL; ISSN: 0957-4530
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A novel hydrogel was prepared by crosslinking hyaluronan with glycol chitosan in aqueous solution using water soluble carbodiimide at nearly neutral pH and room temperature The products can be easily formulated into injectable gels, various films, membranes and sponges for soft tissue augmentation, viscosupplementation, drug delivery, preventing adhesion of post operation, wound dressing and tissue engineering scaffolds. The said hydrogel has high water adsorption property and biostability. Rheololgical results of the gel showed a soft and viscoelastic structure. FTIR further confirmed the formation of amide bonds between carboxyl groups of hyaluronan and amine groups of glycol chitosan and no N-acylurea and other derivs. were identified.

L30 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:850664 CAPLUS
DOCUMENT NUMBER: 145:256285
TITLE: Method for producing cross-linked hyaluronic acid-protein biocomposites
INVENTOR(S): Yang, Chiung-Lin; Chen, Jui-Hsiang; Tsai, Shiao-Wen; Shih, Hsin-Nung; Shih, Lih-Yuann
PATENT ASSIGNEE(S): Industrial Technology Research Institute, Taiwan
SOURCE: U.S. Pat. Appl. Publ., 27pp., Cont.-in-part of U.S. Ser. No. 76,288.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2006189516	A1	20060824	US 2005-208596		20050823
US 2003100739	A1	20030529	US 2002-76288		20020219
PRIORITY APPLN. INFO.:			US 2002-76288	B2	20020219
			TW 2001-90119567	A	20010810

AB This invention is concerned with a new method for producing cross-linked hyaluronic acid-protein biocomposites in various shapes. In the present process, a polysaccharide solution and a protein solution are mixed under moderate pH values in presence of salts to form a homogenous solution, which can be processed into various shapes, such as membrane, sponge, fiber, tube or micro-granular and so on. After then, the homogenous solution is subjected to a crosslinking reaction in organic solvent containing weak acid to produce an implantable biocomposite material having excellent bio-compatibility, biodegradability, prolonged enzymic degradation time, and good phys. properties. Hyaluronic acid (50 mg) was dissolved in 5 mL of pure water. Sep., gelatin (50 mg) was dissolved in 5 mL of warm water and then added with sodium chloride (30 mg). The prepared two solns. were mixed together to form a 10 mL mixture of which pH was around 6.5, the weight ratio of HA to collagen was 1 to 1 and a solid content was 1%. The resulting solution was cast into a mold made of

Teflon and allowed to dry in an oven to yield a transparent film

L30 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1333979 CAPLUS
DOCUMENT NUMBER: 144:74821
TITLE: Process for preparing a crosslinked carboxyl polysaccharide for dosage forms
INVENTOR(S): Young, Jenn-Jong
PATENT ASSIGNEE(S): National Defense Medical Center, Taiwan
SOURCE: U.S. Pat. Appl. Publ., 7 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005281855	A1	20051222	US 2004-872245	20040618
PRIORITY APPLN. INFO.:			US 2004-872245	20040618

AB A process for preparing a cross-linked polysaccharide comprises providing a polysaccharide with free carboxyl and hydroxyl groups capable of forming an intermol. ester bond and crosslinking the polysaccharide by using onium salt, phosphonium salt, uronium (carbenium) salt and in the presence or in the absence of organic base as crosslinking reagent to obtain a highly crosslinked polysaccharide. The crosslinked polysaccharide film produced has high crosslinking d., is stable and slowly biodegradable in the presence of hydrolysis enzyme, and retains 80% of its original weight after standing in PBS (pH 7.4) at 37° for at least 4 wk. For example, 30 g of hyaluronic acid (HA) 2 weight% viscous solution, poured into a petri dish, was lyophilized at -35° for 3 days, resulting in a primrose yellow HA sponge. HA sponge was weighed and directly immersed in an ethanol/water mixture (8:2 volume/volume) containing 1 equiv (molar ratios of a reagent based on the carboxylate groups in alginate) of 25 mM 2-chloro-1-methylpyridinium iodide (CMPI) and triethylamine, then shaken at room temperature for 3 days. The crosslinked sponge was washed with 80% ethanol and 20 mL water was added to make the crosslinked sponges absorb the water and swell. The sponge was lyophilized at -35° for 3 days and resulted in a primrose yellow crosslinked HA sponge.

L30 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:14271 CAPLUS
DOCUMENT NUMBER: 142:100475
TITLE: Adhesion inhibiting material for vertebral/spinal operation
INVENTOR(S): Haro, Hirotaka; Kato, Takeshi; Miyoshi, Teruzou; Miyata, Yoshiaki; Umeda, Toshihiko
PATENT ASSIGNEE(S): Denki Kagaku Kogyo Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000374	A1	20050106	WO 2004-JP9750	20040630

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

EP 1640026 A1 20060329 EP 2004-747218 20040630
R: DE, FR, GB, IT
PRIORITY APPLN. INFO.: JP 2003-186760 A 20030630
WO 2004-JP9750 W 20040630

AB It is intended to provide a spongy, filmy or suspension material for inhibiting vertebral/spinal adhesion to be employed for assisting or promoting tissue healing. Namely, a spongy, filmy or suspension material for inhibiting adhesion in a vertebral/spinal operation that is to be employed for relieving or inhibiting adhesion caused by a vertebral/spinal operation and contains a crosslinked acidic polysaccharide. Thus, crosslinked hyaluronic acid sponge with a pore size of 120 ± 45 μm and a thickness of 4 mm was prepared from sodium hyaluronate.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:29537 CAPLUS
DOCUMENT NUMBER: 138:78545
TITLE: Hyaluronic acid gel-based cell culture substrates for tissue regeneration
INVENTOR(S): Kato, Yukio; Tsutsumi, Shinichi; Miyazaki, Kazuko; Hara, Maiko; Kawaguchi, Hiroyuki; Kurihara, Hidemi; Miyoshi, Shozo; Hashimoto, Masamichi; Himeta, Koichi
PATENT ASSIGNEE(S): Denki Kagaku Kogyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003010308	A2	20030114	JP 2001-196687	20010628

PRIORITY APPLN. INFO.: JP 2001-196687 20010628

AB The substrate is made of hyaluronic acid (I) gel which is not substantially modified with chemical crosslinking agents or chemical modifying agents and is slightly-soluble in neutral aqueous solution Animal cells, e.g. chondrocytes, stem cells, bone marrow cells, osteoblasts, ES cells, etc., are disseminated on the substrate and the substrate containing the surviving cells is applied to defective parts of tissues to regenerate tissues, e.g. articular cartilage, costal cartilage, tracheal cartilage, skull, periodontium, cementum tendon, ligament, etc. The gel may be in the forms of sheets, films, sponges, fibers, tubes, etc., and contain bioactive substances such as cell growth factors, antibiotics, proteins, oligosaccharides, or nucleic acids. I with mol. weight 2 + 106 dalton was dissolved in H2O and the solution was adjusted to pH 1.5 with HNO3 and frozen in a flat-bottomed container at -20° for 5 days. The frozen product was soaked in a phosphate-buffered saline solution for 24 h and dried to give sponge-like gel. Rabbit femur- and tibia-derived mesenchymal cells (preparation given) were disseminated on the gel and incubated to become confluent in the presence of bFGF. Subculture was repeated twice and the 3rd subculture was implanted into a

drilled hole formed in knee articular cartilage of a rabbit to promote regeneration of cartilage and bone.

L30 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:531123 CAPLUS
DOCUMENT NUMBER: 137:83718
TITLE: Wound dressings comprising nonwoven fabrics, thermoplastic films, and sponge layers
INVENTOR(S): Komazawa, Takao
PATENT ASSIGNEE(S): Toyobo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002200110	A2	20020716	JP 2001-1616	20010109
PRIORITY APPLN. INFO.:			JP 2001-1616	20010109

AB The dressings comprise (a) nonwoven fabric layers consisting of hydrophobic fibers and superabsorbent fibers, (b) porous thermoplastic (other than polyurethane) films, and (c) uncrosslinked hyaluronic acid sponge layers. The dressings show good liquid absorption and water release. Polyester-rayon needle-punched nonwoven fabric containing Ag sulfadiazine, polyester film (Pelprene), and uncrosslinked hyaluronic acid sponge were laminated to give a wound dressing.

L30 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:160205 CAPLUS
DOCUMENT NUMBER: 136:221766
TITLE: Superabsorbent and water-releasing wound dressings
INVENTOR(S): Komazawa, Takao
PATENT ASSIGNEE(S): Toyobo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002065722	A2	20020305	JP 2000-265853	20000901
PRIORITY APPLN. INFO.:			JP 2000-265853	20000901

AB The wound dressings comprise a nonwoven fabric layer of hydrophobic fibers and superabsorbent fibers, a polyurethane film layer having open pores, and a noncrosslinked hyaluronic acid sponge layer. A wound dressing comprising a polyester-rayon nonwoven fabric layer containing Ag sulfadiazine, a polyurethane film prepared from polytetramethylene glycol, dicyclohexylmethane 4,4'-diisocyanate, and isophorone diamine, and a noncrosslinked hyaluronic acid layer promoted wound healing in rats.

L2 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:694981 CAPLUS
DOCUMENT NUMBER: 143:482971
TITLE: Implantation of preadipocyte-loaded hyaluronic acid-based scaffolds into nude mice to evaluate potential for soft tissue engineering
AUTHOR(S): Hemmrich, Karsten; von Heimburg, Dennis; Rendchen, Raoul; Di Bartolo, Chiara; Milella, Eva; Pallua, Norbert
CORPORATE SOURCE: Department of Plastic Surgery and Hand Surgery, University Hospital of the Aachen University of Technology, Aachen, D-52057, Germany
SOURCE: Biomaterials (2005), 26(34), 7025-7037
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The reconstruction of soft tissue defects following extensive deep burns or tumor resections remains an unresolved problem in plastic and reconstructive surgery since adequate implant materials are still not available. Preadipocytes, immature precursor cells found between mature adipocytes in adipose tissue, are a potential material for soft tissue engineering since they can proliferate and differentiate into adipose tissue after transplantation. In previous studies, the authors identified hyaluronan benzyl ester (HYAFF-11) sponges to be promising carrier matrixes. This study now evaluates, in vitro and in vivo, a new sponge architecture with pores of 400 μm either made of plain HYAFF-11 or HYAFF-11 coated with the extracellular matrix glycosaminoglycan hyaluronic acid. Human preadipocytes were isolated, seeded onto carriers and implanted into nude athymic mice. Explants harvested after 3, 8, and 12 wk were examined for macroscopical appearance, thickness, weight, pore structure, histol., and immunohistochem. Compared to previous studies, the authors found better penetration of cells into both types of scaffolds, with more extensive formation of new vessels throughout the construct but with only minor adipose tissue. The authors' encouraging results contribute towards a better seeded and vascularized scaffold but also show that the enhancement of adipogenic conversion of preadipocytes remains a major task for further in vivo expts.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 2 MEDLINE on STN
ACCESSION NUMBER: 2005400405 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15964623
TITLE: Implantation of preadipocyte-loaded hyaluronic acid-based scaffolds into nude mice to evaluate potential for soft tissue engineering.
AUTHOR: Hemmrich Karsten; von Heimburg Dennis; Rendchen Raoul; Di Bartolo Chiara; Milella Eva; Pallua Norbert
CORPORATE SOURCE: Department of Plastic Surgery and Hand Surgery, Burn Centre, University Hospital of the Aachen University of Technology, Germany.
SOURCE: Biomaterials, (2005 Dec) Vol. 26, No. 34, pp. 7025-37.
Journal code: 8100316. ISSN: 0142-9612.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200512
ENTRY DATE: Entered STN: 3 Aug 2005
Last Updated on STN: 15 Dec 2005
Entered Medline: 7 Dec 2005

AB The reconstruction of soft tissue defects following extensive deep burns or tumor resections remains an unresolved problem in plastic and reconstructive surgery since adequate implant materials are still not available. Preadipocytes, immature precursor cells found between mature adipocytes in adipose tissue, are a potential material for soft tissue engineering since they can proliferate and differentiate into adipose tissue after transplantation. In previous studies, we identified hyaluronan benzyl ester (HYAFF 11) sponges to be promising carrier matrices. This study now evaluates, in vitro and in vivo, a new sponge architecture with pores of 400 microm either made of plain HYAFF 11 or HYAFF 11 coated with the extracellular matrix glycosaminoglycan hyaluronic acid. Human preadipocytes were isolated, seeded onto carriers and implanted into nude athymic mice. Explants harvested after 3, 8, and 12 weeks were examined for macroscopical appearance, thickness, weight, pore structure, histology, and immunohistochemistry. Compared to previous studies, we found better penetration of cells into both types of scaffolds, with more extensive formation of new vessels throughout the construct but with only minor adipose tissue. Our encouraging results contribute towards a better seeded and vascularised scaffold but also show that the enhancement of adipogenic conversion of preadipocytes remains a major task for further in vivo experiments.

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L1             0 S ENZYL? (P) HYALURONIC ACID (P) TUMOR?
L2             2 S BENZYL? (P) HYALURONIC ACID (P) TUMOR?
L3             2 S ?BENZYL? (P) HYALURONIC ACID (P) TUMOR?
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L3             2 S ?BENZYL? (P) HYALURONIC ACID (P) TUMOR?
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L4 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:1221768 CAPLUS
TITLE: Antitumor sustained-release injection containing platinum compounds and/or their synergistic agents from phosphoinositide-3-kinase inhibitor, pyrimidine analog, and/or dna repairase inhibitor
INVENTOR(S): Kong, Qingzhong; Zhang, Hongjun; Yu, Jianjiang
PATENT ASSIGNEE(S): Shandong Lan-Jin Bioengineering Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 33pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1861050	A	20061115	CN 2006-10200585	20060621
PRIORITY APPLN. INFO.:			CN 2006-10200585	20060621

AB The patent antitumor sustained-release injection is comprised of (A) sustained-release microsphere comprising antitumor effective constituent 0.5-60 wt%, and sustained-release adjuvant 40-99 wt%, and suspending agent 0.0-30 wt%; and (B) solvent. The antitumor effective constituent is platinum compds. and/or their synergistic agents from phosphoinositide-3-kinase inhibitor, pyrimidine analog, and/or DNA repairase inhibitor. The platinum compds. are selected from selected from sunpla, eptaplatin, bicycloplatin, citricplatin, and picoplatin. The phosphoinositide-3-kinase inhibitor is selected from one of 7-hydroxyl-staurosporine, 7-oxy-alkyl-staurosporine, β-methoxyl staurosporine, etc., or the mixture thereof. The pyrimidine analog is selected from one of 04-benzyl folic acid, 2,4,5-triamino-6-benzyloxy pyrimidine, 2,4-diamino-6-benzyloxy -5-nitrosopyrimidine, 2-amino-O-4-benzyl pteridine, etc., or the mixture thereof. The DNA repairase inhibitor is selected from one of (a) 2-(morphol-4-yl)-benzo[h]chromone-4-one, 2-(4-morpholinyl)-8-Ph chromone, etc.; (b) 3-aminobenzamide, benzamide, 3,4-dihydro methoxyisoquinolin-1(2H)-benzamide, etc.; and (c) aminotriazole, DL-buthionine(S,R)-sulfoximine, calvatic acid, S-hexyl glutathione, etc. The sustained-release adjuvant is selected from one of a) polylactic acid; b) Polyglycolic acid-hydroxy acetic acid copolymer; c) polifeprosan; d) ethene-vinyl acetate copolymer; e) difatty acid-sebacic acid copolymer; f) poly(erucic acid dimer-sebacic acid) copolymer; g) poly(fumaric acid-sebacic acid) copolymer; h) sodium CM-cellulose, hydroxypropyl cellulose, xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, etc.; or i) racemic polylactic acid, etc., or the mixture thereof. The suspending agent is one of a) 0.5-3.0 % (sodium) CM-cellulose; b) 5-15 % mannitol; c) 5-15 % sorbitol; d) 0.1-1.5 % surfactant; e) 0.1-0.5 % tween 20; f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; g) 0.5-5 % sodium CM-cellulose + 0.1-0.5 % tween 80; h) 5-20 % mannitol + 0.1-0.5 % tween 80; or i) 0.5-5 % sodium CM-cellulose + 5-20 % sorbitol + 0.1-0.5 % tween 80. Said sustained-release preparation can reduce toxic reaction, at the same time can increase selectively drug concentration, and enhance therapeutic effectiveness.

L4 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:1221763 CAPLUS
TITLE: Gemcitabine antitumor sustained-release injection containing anti-metabolic drug and/or its synergistic agent from phosphoinositide-3-kinase inhibitor, pyrimidine analog, and/or dna repairase inhibitor
INVENTOR(S): Kong, Qingzhong; Sun, Juan; Liu, Yuyan; Song,

Bangqiang
PATENT ASSIGNEE(S): Shandong Lan-Jin Bioengineering Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 34pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1861049	A	20061115	CN 2006-10200256	20060317

PRIORITY APPLN. INFO.: CN 2006-10200256 20060317

AB The patent antitumor sustained-release injection is comprised of (A) sustained-release microsphere comprising antitumor effective constituent 0.5-60 wt%, and sustained-release adjuvant 40-99 wt%, and suspending agent 0.0-30 wt%; and (B) solvent. The antitumor effective constituent is anti-metabolic drug and/or its synergistic agent from phosphoinositide-3-kinase inhibitor, pyrimidine analog, and/or DNA repairase inhibitor. The anti-metabolic antitumor drug is selected from alimta, alimta disodium, carmofur, tegafur, zalcitabine, etc. The phosphoinositide-3-kinase inhibitor is selected from one of 7-hydroxyl-staurosporine, 7-oxy-alkyl-staurosporine, β-methoxyl staurosporine, etc., or the mixture thereof. The pyrimidine analog is selected from one of 04-benzyl folic acid, 2,4,5-triamino-6-benzyloxy pyrimidine, 2,4-diamino-6-benzyloxy -5-nitrosopyrimidine, 2-amino-O-4-benzyl pteridine, etc., or the mixture thereof. The DNA repairase inhibitor is selected from one of (a) 2-(morphol-4-yl)-benzo[h]chromone-4-one, 2-(4-morpholinyl)-8-Ph chromone, etc.; (b) 3-aminobenzamide, benzamide, 3,4-dihydro methoxyisoquinolin-1(2H)-benzamide, etc.; and (c) aminotriazole, DL-buthionine(S,R)-sulfoximine, calvatic acid, S-hexyl glutathione, etc. The sustained-release adjuvant is selected from one of a) polylactic acid; b) Polyglycolic acid-hydroxy acetic acid copolymer; c) polifeprosan; d) ethene-vinyl acetate copolymer; e) difatty acid-sebacic acid copolymer; f) poly(erucic acid dimer-sebacic acid) copolymer; g) poly(fumaric acid-sebacic acid) copolymer; h) sodium CM-cellulose, hydroxypropyl cellulose, xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, etc.; or i) racemic polylactic acid, etc., or the mixture thereof. The suspending agent is one of a) 0.5-3.0 % (sodium) CM-cellulose; b) 5-15 % mannitol; c) 5-15 % sorbitol; d) 0.1-1.5 % surfactant; e) 0.1-0.5 % tween 20; f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; g) 0.5-5 % sodium CM-cellulose + 0.1-0.5 % tween 80; h) 5-20 % mannitol + 0.1-0.5 % tween 80; or i) 0.5-5 % sodium CM-cellulose + 5-20 % sorbitol + 0.1-0.5 % tween 80. Said sustained-release preparation can reduce toxic reaction, at the same time can increase selectively drug concentration, and enhance therapeutic effectiveness.

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:1221757 CAPLUS
TITLE: Antitumor sustained-release injection containing vascular inhibitor and its synergistic agent from phosphoinositide-3-kinase inhibitor, pyrimidine analog, and/or dna repairase inhibitor
INVENTOR(S): Sun, Zhongxian
PATENT ASSIGNEE(S): Jinan Shuaihua Pharmaceutical Science and Technology Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 34pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1861047	A	20061115	CN 2006-10200196	20060306

PRIORITY APPLN. INFO.: CN 2006-10200196 20060306

AB The patent antitumor sustained-release injection is comprised of (A) sustained-release microsphere comprising antitumor effective constituent 0.5-60 wt%, and sustained-release adjuvant 40-99 wt%, and suspending agent 0.0-30 wt%; and (B) solvent. The antitumor effective constituent is vascular inhibitor and its synergistic agent from phosphoinositide-3-kinase inhibitor, pyrimidine analog, and/or DNA repairase inhibitor. The vascular inhibitor is selected form one of gefitinib, tarceva, lapatinib, angiostatin, avastin, canertinib, panitumumab, or the mixture thereof. The phosphoinositide-3-kinase inhibitor is selected from one of 7-hydroxyl-staurosporine, 7-oxy-alkyl-staurosporine, β-methoxyl staurosporine, etc., or the mixture thereof. The pyrimidine analog is selected from one of 04-benzyl folic acid, 2,4,5-triamino-6-benzyloxy pyrimidine, 2,4-diamino-6-benzyloxy-5-nitrosopyrimidine, 2-amino-O-4-benzyl pteridine, etc., or the mixture thereof. The DNA repairase inhibitor is selected from one of (a) 2-(morphol-4-yl)-benzo[h]chromone-4-one, 2-(4-morpholinyl)-8-Ph chromone, etc.; (b) 3-aminobenzamide, benzamide, 3,4-dihydro methoxyisoquinolin-1(2H)-benzamide, etc.; and (c) aminotriazole, DL-buthionine(S,R)-sulfoximine, calvatic acid, S-hexyl glutathione, etc. The sustained-release adjuvant is selected from one of a) polylactic acid; b) Polyglycolic acid-hydroxy acetic acid copolymer; c) polifeprosan; d) ethene-vinyl acetate copolymer; e) difatty acid-sebacic acid copolymer; f) poly(erucic acid dimer-sebacic acid) copolymer; g) poly(fumaric acid-sebacic acid) copolymer; h) sodium CM-cellulose, hydroxypropyl cellulose, xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, etc.; or i) racemic polylactic acid, etc., or the mixture thereof. The suspending agent is one of a) 0.5-3.0 % (sodium) CM-cellulose; b) 5-15 % mannitol; c) 5-15 % sorbitol; d) 0.1-1.5 % surfactant; e) 0.1-0.5 % tween 20; f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; g) 0.5-5 % sodium CM-cellulose + 0.1-0.5 % tween 80; h) 5-20 % mannitol + 0.1-0.5 % tween 80; or i) 0.5-5 % sodium CM-cellulose + 5-20 % sorbitol + 0.1-0.5 % tween 80. Said sustained-release preparation can reduce toxic reaction, at the same time can increase selectively drug concentration, and enhance therapeutic effectiveness.

L4 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:1202128 CAPLUS

TITLE: Antitumor sustained-release injection containing anti-metabolic antitumor drug and/or its synergistic agent from alkylating agent and/or guanine analogs

INVENTOR(S): Kong, Qingzhong; Sun, Juan; Zhang, Hongjun; Chen, Ying

PATENT ASSIGNEE(S): Shandong Lan-Jin Bioengineering Co., Ltd., Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 31pp. CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1857209	A	20061108	CN 2006-10200258	20060317

PRIORITY APPLN. INFO.: CN 2006-10200258 20060317

AB The sustained-release injection is comprised of (A) sustained-release microsphere comprising antitumor effective constituent 0.5-60, sustained-release adjuvant 40-99 wt% and suspending agent 0.0-30 wt%; and

(B) solvent. The antitumor effective constituent is selected from anti-metabolic antitumor drug and/or its synergistic agent which is alkylating agent and/or purine analogs. The anti-metabolic antitumor drugs are selected from alimta, alimta disodium, carmofur, tegafur, zalcitabine, etc. The guanine analogs are selected from, O6-benzyl guanine, O6-Bu guanine, O6-Me guanine, O6-alkyl guanine, O6-benzyl uric acid or O6-benzyl xanthine. The alkylating agent is selected from one of ambamustine, nimustine, bendamustine, lomustine, tallimustine, melphalan, etc., or the mixture thereof. The sustained-release adjuvant is selected from one of a) polylactic acid; b) Polyglycolic acid-hydroxy acetic acid copolymer; c) polifeprosan; d) ethene-vinyl acetate copolymer; e) difatty acid-sebacic acid copolymer; f) poly(erucic acid dimer-sebacic acid) copolymer; g) poly(fumaric acid-sebacic acid) copolymer; h) sodium CM-cellulose, hydroxypropyl cellulose, xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, etc.; or the mixture thereof. The suspending agent is one of a) 0.5-3.0 % (sodium) CM-cellulose; b) 5-15 % mannitol; c) 5-15 % sorbitol; d) 0.1-1.5 % surfactant; e) 0.1-0.5 % tween 20; f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; g) 0.5-5 % sodium CM-cellulose + 0.1-0.5 % tween 80; h) 5-20 % mannitol + 0.1-0.5 % tween 80; or i) 0.5-5 % sodium CM-cellulose + 5-20 % sorbitol + 0.1-0.5 % tween 80.

L4 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:1144397 CAPLUS
TITLE: Antitumor sustained-release injection containing platinum compound and/or its synergistic agent
INVENTOR(S): Kong, Qinglun
PATENT ASSIGNEE(S): Jinan Shuaihua Pharmaceutical Science and Technology Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 29pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1850043	A	20061025	CN 2006-10200142	20060220

PRIORITY APPLN. INFO.: CN 2006-10200142 20060220

AB The sustained-release injection is comprised of (A) sustained-release microsphere comprising antitumor effective constituent 0.5-60, sustained-release adjuvant 41-99.9 and suspending agent 0.0-30 wt%; and (B) solvent. The antitumor effective constituent is selected from platinum compound and/or its synergistic agent which is selected from phosphoinositide-3-kinase inhibitor, guanine analog, tetrazine compound and/or platinum compound Said platinum drug is selected from cisplatin, carboplatin, ormaplatin, dexormaplatin, hetaplatin, lobaplatin, nedaplatin or oxaliplatin. Said phosphoinositide-3-kinase inhibitor is selected from one of 7-hydroxyl-staurosporine, 7-oxy-alkyl-staurosporine, β-methoxyl staurosporine, etc., or the mixture thereof. Said guanine analog is selected from benzyl guanine, O6-benzyl guanine, O6-Bu guanine, O6-Me guanine, O6-alkyl guanine, etc. Said tetrazine compound is selected from imidazo tetrazine, imidazo pyrazine, 1-hydrogen-imidazo[b]pyrazine, imidazopyridine, 1-hydrogen-imidazo[1,2-a]pyridine, procarbazine, mitozolomide, dacarbazine, and temozolomide. The sustained-release adjuvant is selected from one of a) polylactic acid; b) Polyglycolic acid-hydroxy acetic acid copolymer; c) polifeprosan; d) ethene-vinyl acetate copolymer; e) difatty acid-sebacic acid copolymer; f) poly(erucic acid dimer-sebacic acid) copolymer; g) poly(fumaric acid-sebacic acid) copolymer, xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, etc.; or the mixture thereof. The suspending agent is one of a) 0.5-3.0 % (sodium)

CM-cellulose; b) 5-15 % mannitol; c) 5-15 % sorbitol; d) 0.1-1.5 % surfactant; e) 0.1-0.5 % tween 20; f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; g) 0.5-5 % sodium CM-cellulose + 0.1-0.5 % tween 80; h) 5-20 % mannitol + 0.1-0.5 % tween 80; or i) 0.5-5 % sodium CM-cellulose + 5-20 % sorbitol + 0.1-0.5 % tween 80, or the mixture thereof.

L4 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:1144333 CAPLUS
TITLE: Compound platinum antitumor sustained-release injection
INVENTOR(S): Kong, Qinglun
PATENT ASSIGNEE(S): Jinan Shuaihua Pharmaceutical Science and Technology Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 35pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1850039	A	20061025	CN 2006-10200138	20060220

PRIORITY APPLN. INFO.: CN 2006-10200138 20060220

AB The sustained-release injection is comprised of (A) sustained-release microsphere comprising antitumor effective constituent 0.5-60, sustained-release adjuvant 40-99 wt% and suspending agent 0.0-30 wt%; and (B) solvent. The antitumor effective constituent is selected from platinum drug and/or its synergistic agent which is selected from phosphoinositide-3-kinase inhibitor, pyrimidine analog, and/or DNA repairase inhibitor. The platinum drug is selected from cisplatin, carboplatin, ormaplatin, dexormaplatin, hetaplatin, lobaplatin, nedaplatin or oxaliplatin. The phosphoinositide-3-kinase inhibitor is selected from one of 7-hydroxyl-staurosporine, 7-oxy-alkyl-staurosporine, β-methoxyl staurosporine, etc., or the mixture thereof. The pyrimidine analog is selected from one of 04-benzyl folic acid, 2,4,5-triamino-6-benzyloxy pyrimidine, 2,4-diamino-6-benzyloxy-5-nitrosopyrimidine, 2-amino-0-4-benzyl pteridine, etc., or the mixture thereof. The DNA repairase inhibitor is selected from one of (a) imidazo pyrazine, imidazopyridine, wortmannin, Benzochromanone, 2-(morpholine-4-yl)-benzo[h]chomen-4-one, etc.; (b) 3-aminobenzamide, benzamide, 3,4-dihydro-5-methoxyisoquinolin-1(2H)-benzamide, etc.; and (c) aminotriazole, DL-buthionine(S,R)-sulfoximine, calvatic acid, S-hexyl glutathione, etc. The sustained-release adjuvant is selected from one of a) polylactic acid; b) Polyglycolic acid-hydroxy acetic acid copolymer; c) polifeprosan; d) ethene-vinyl acetate copolymer; e) difatty acid-sebacic acid copolymer; f) poly(erucic acid dimer-sebacic acid) copolymer; g) poly(fumaric acid-sebacic acid) copolymer; h) sodium CM-cellulose, hydroxypropyl cellulose, xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, etc.; or the mixture thereof. The suspending agent is one of a) 0.5-3.0 % (sodium) CM-cellulose; b) 5-15 % mannitol; c) 5-15 % sorbitol; d) 0.1-1.5 % surfactant; e) 0.1-0.5 % tween 20; f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; g) 0.5-5 % sodium CM-cellulose + 0.1-0.5 % tween 80; h) 5-20 % mannitol + 0.1-0.5 % tween 80; or i) 0.5-5 % sodium CM-cellulose + 5-20 % sorbitol + 0.1-0.5 % tween 80, or the mixture thereof.

L4 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:1112813 CAPLUS
DOCUMENT NUMBER: 145:495542
TITLE: Antitumor sustained-release injection containing taxane and its synergistic agent
INVENTOR(S): Liu, Yuyan
PATENT ASSIGNEE(S): Jinan Kangquan Pharmaceutical Science and Technology

Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 35pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1846687	A	20061018	CN 2006-10200112	20060210

PRIORITY APPLN. INFO.: CN 2006-10200112 20060210

AB The patent antitumor sustained-release injection is comprised of (A) sustained-release microsphere comprising antitumor effective constituent 0.5-60%, sustained-release adjuvant 40-99% and suspending agent 0.0-30.0%; and (B) solvent. The antitumor effective constituent is taxane and taxane synergistic agent which is selected from phosphoinositide-3-kinase inhibitor, pyrimidine analogs and/or DNA repair enzyme inhibitor. Said taxane is selected from taxol, docetaxel, paclitaxel-2'-hydroxy, 10-deacetylbaccatin III, and 7-epi-taxol. Said phosphoinositide-3-kinase inhibitor is selected from one of 7-hydroxyl-staurosporine, 7-oxy-alkyl-staurosporine, β-methoxyl staurosporine, etc., or the mixture thereof. Said pyrimidine analog is selected from one of 04-benzyl folic acid, 2,4,5-triamino-6-benzyloxy pyrimidine, 2,4-diamino-6-benzyloxy -5-nitrosopyrimidine, 2-amino-O-4-benzyl pteridine, etc., or the mixture thereof. Said DNA repair enzyme inhibitor is selected from one of (a) imidazo pyrazine, imidazopyridine, Wortmannin, Benzochromenone, 2-(morpholine-4-yl)-benzo[h]chomen-4-one, etc.; (b) 3-aminobenzamide, benzamide, 3,4-dihydro-5-methoxyisoquinolin-1(2H)-benzamide, etc.; and (c) aminotriazole, DL-buthionine(S,R)-sulfoximine, Calvatic acid, S-hexyl glutathione, etc. The sustained-release adjuvant is selected from one of (a) polylactic acid; (b) Polyglycolic acid-hydroxy acetic acid copolymer; (c) polifeprosan; (d) ethene-vinyl acetate copolymer; (e) difatty acid-sebacic acid copolymer; (f) poly(erucic acid dimer-sebacic acid) copolymer; (g) poly(fumaric acid-sebacic acid) copolymer, xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, gelatin, etc.; or the mixture thereof. The suspending agent is one of (a) 0.5-3.0 % (sodium) CM-cellulose; (b) 5-15 % mannitol; (c) 5-15 % sorbitol; (d) 0.1-1.5 % surfactant; (e) 0.1-0.5 % tween 20; (f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; (g) 0.5-5 % sodium CM-cellulose + 0.1-0.5 % tween 80; (h) 5-20 % mannitol + 0.1-0.5 % tween 80; or (i) 0.5-5 % sodium CM-cellulose + 5-20 % sorbitol + 0.1-0.5 % tween 80. Said sustained-release preparation can reduce toxic reaction, at the same time can increase selectively drug concentration, and enhance therapeutic effectiveness.

L4 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:1112810 CAPLUS
DOCUMENT NUMBER: 145:495541
TITLE: Antitumor sustained-release injection containing taxane and its synergistic agent
INVENTOR(S): Liu, Yuyan
PATENT ASSIGNEE(S): Jinan Kangquan Pharmaceutical Science and Technology Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 34pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

CN 1846686	A	20061018	CN 2006-10200110	20060210
PRIORITY APPLN. INFO.:			CN 2006-10200110	20060210

AB The patent antitumor sustained-release injection is comprised of (A) sustained-release microsphere comprising antitumor effective constituent 0.5-60%, sustained-release adjuvant 40-99% and suspending agent 0.0-30.0%; and (B) solvent. The antitumor effective constituent is taxane and taxane synergistic agent which is selected from topoisomerase inhibitors, guanine analogs, tetrazine compds., and platinum compds. Said topoisomerase inhibitor is selected from one of camptothecin, hydroxycamptothecine, lurtotecan, topotecan, irinotecan, etc., or the mixture thereof. Said guanine drug is selected from benzyl guanine, O6-benzyl guanine, O6-Bu guanine, O6-Me guanine, O6-alkyl guanine, etc. or the mixture thereof. Said platinum compound is selected from one of cisplatin, cycloplatin, sunplatinum, dacarbazine, nedaplatin, ormaplatin, zeniplatin, etc. Said tetrazine compound is selected from one of imidazotetrazine, imidazopyridine, 1-hydrogen-imidazo[b]pyrazine, imidazopyridine, 1-hydrogen-imidazo[1,2-a]pyridinium, procarbazine, mitozolomide, dacarbazine, temozolomide, or the mixture thereof. Said platinum compound is selected from one of cisplatin, cycloplatin, sunplatinum, dacarbazine, nedaplatin, or ormaplatin. The sustained-release adjuvant is selected from one of (a) polylactic acid; (b) Polyglycolic acid-hydroxy acetic acid copolymer; (c) polifeprosan; (d) ethene-vinyl acetate copolymer; (e) difatty acid-sebacic acid copolymer; (f) poly(erucic acid dimer-sebacic acid) copolymer; (g) poly(fumaric acid-sebacic acid) copolymer, xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, gelatin, etc.; or the mixture thereof. The suspending agent is one of (a) 0.5-3.0 % (sodium) CM-cellulose; (b) 5-15 % mannitol; (c) 5-15 % sorbitol; (d) 0.1-1.5 % surfactant; (e) 0.1-0.5 % tween 20; (f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; (g) 0.5-5 % sodium CM-cellulose + 0.1-0.5 % tween 80; (h) 5-20 % mannitol + 0.1-0.5 % tween 80; or (i) 0.5-5 % sodium CM-cellulose + 5-20 % sorbitol + 0.1-0.5 % tween 80. Said sustained-release preparation can reduce toxic reaction, at the same time can increase selectively drug concentration, and enhance therapeutic effectiveness.

L4 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2006:1112807 CAPLUS
DOCUMENT NUMBER:	145:495540
TITLE:	Antitumor sustained-release injection containing bendamustine and its synergistic agent
INVENTOR(S):	Kong, Qingxia
PATENT ASSIGNEE(S):	Jinan Shuaihua Pharmaceutical Science and Technology Co., Ltd., Peop. Rep. China
SOURCE:	Faming Zhuanli Shenqing Gongkai Shuomingshu, 28pp. CODEN: CNXXEV
DOCUMENT TYPE:	Patent
LANGUAGE:	Chinese
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1846685	A	20061018	CN 2006-10200078	20060125
PRIORITY APPLN. INFO.:			CN 2006-10200078	20060125

AB The title antitumor sustained-release injection is comprised of (A) sustained-release microsphere comprising antitumor effective constituent 0.5-60%, sustained-release adjuvant 40-99% and suspending agent 0.0-30.0%; and (B) solvent. The antitumor effective constituent is bendamustine or the combination of bendamustine and its synergistic agent which is selected from topoisomerase inhibitors, guanine analogs, tetrazine compds., and platinum compds. Said platinum compound is selected from one of cisplatin, cycloplatin, sunplatinum, dacarbazine, nedaplatin, ormaplatin, zeniplatin, etc. Said topoisomerase inhibitor is

selected from one of camptothecin, hydroxycamptothecine, lurtotecan, topotecan, irinotecan, etc., or the mixture thereof. Said guanines drug is selected from benzyl guanine, O6-benzyl guanine, O6-Bu guanine, O6-Me guanine, O6-alkyl guanine, etc. or the mixture thereof. Said tetrazine compound is selected from one of imidazo tetrazine, imidazopyridine, 1-hydrogen-imidazo[b]pyrazine, imidazopyridine, 1-hydrogen-imidazo[1,2-a]pyridinium, procarbazine, mitozolomide, dacarbazine, temozolomide, or the mixture thereof. Said platinum compound is selected from one of cisplatin, cycloplatin, sunplatinum, dacarbazine, nedaplatin, or ormaplatin, etc. The sustained-release adjuvant is selected from one of (a) polylactic acid; (b) Polyglycolic acid-hydroxy acetic acid copolymer; (c) polifeprosan; (d) ethene-vinyl acetate copolymer; (e) difatty acid-sebacic acid copolymer; (f) poly(erucic acid dimer-sebacic acid) copolymer; (g) poly(fumaric acid-sebacic acid) copolymer, xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, gelatin, etc.; or the mixture thereof. The suspending agent is one of (a) 0.5-3.0 % (sodium) CM-cellulose; (b) 5-15 % mannitol; (c) 5-15 % sorbitol; (d) 0.1-1.5 % surfactant; (e) 0.1-0.5 % tween 20; (f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; (g) 0.5-5 % sodium CM-cellulose + 0.1-0.5 % tween 80; (h) 5-20 % mannitol + 0.1-0.5 % tween 80; or (i) 0.5-5 % sodium CM-cellulose + 5-20 % sorbitol + 0.1-0.5 % tween 80. Said sustained-release preparation can reduce toxic reaction, at the same time can increase selectively drug concentration, and enhance therapeutic effectiveness.

L4 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:220544 CAPLUS
DOCUMENT NUMBER: 144:338105
TITLE: Angiostatic and guanine analog composite antitumor implanting agent
INVENTOR(S): Kong, Qingzhong; Sun, Juan; Chen, Ying
PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 20 pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1733306	A	20060215	CN 2005-10044376	20050805
PRIORITY APPLN. INFO.:			CN 2005-10044376	20050805

AB The antitumor implanting agent is composed of angiostatic agent 5-30, antitumor agent 5-30, and medical adjuvant to 100%. The angiostatic agent is carboxyamidotriazole, thalidomide, linomide, angiostatin, endostatin, vascular endothelial growth factor receptor inhibitor, imatinib mesylate, semaxanib, gefitinib, erlotinib, etc. The antitumor agent is guanine, O6-benzylguanine, O6-butylguanine, O6-methylguanine, O6-alkylguanine, 2-amino-6-oxypurine, O6-benzyl-2'-deoxyguanosine, 8-amino-O6-benzylguanine, 8-hydroxy-O6-benzylguanine, 8-bromo-O6-benzylguanine, etc. The medical adjuvant is polylactic acid, ethylene-vinyl acetate copolymer, xylitol, oligosaccharide, chitin, hyaluronic acid, chondroitin sulfate, etc. The dosage form of the antitumor implanting agent is suspension, release sustaining agent, implant, and release sustaining implant. The systemic toxic reaction of the antitumor agent is decreased and the local concentration of the antitumor agent is increased by local administration, so the pharmacol. effect is increased.

L4 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:694981 CAPLUS
DOCUMENT NUMBER: 143:482971

TITLE: Implantation of preadipocyte-loaded hyaluronic acid-based scaffolds into nude mice to evaluate potential for soft tissue engineering
AUTHOR(S): Hemmrich, Karsten; von Heimburg, Dennis; Rendchen, Raoul; Di Bartolo, Chiara; Milella, Eva; Pallua, Norbert
CORPORATE SOURCE: Department of Plastic Surgery and Hand Surgery, University Hospital of the Aachen University of Technology, Aachen, D-52057, Germany
SOURCE: Biomaterials (2005), 26(34), 7025-7037
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The reconstruction of soft tissue defects following extensive deep burns or tumor resections remains an unresolved problem in plastic and reconstructive surgery since adequate implant materials are still not available. Preadipocytes, immature precursor cells found between mature adipocytes in adipose tissue, are a potential material for soft tissue engineering since they can proliferate and differentiate into adipose tissue after transplantation. In previous studies, the authors identified hyaluronan benzyl ester (HYAFF-11) sponges to be promising carrier matrixes. This study now evaluates, in vitro and in vivo, a new sponge architecture with pores of 400 μm either made of plain HYAFF-11 or HYAFF-11 coated with the extracellular matrix glycosaminoglycan hyaluronic acid. Human preadipocytes were isolated, seeded onto carriers and implanted into nude athymic mice. Explants harvested after 3, 8, and 12 wk were examined for macroscopical appearance, thickness, weight, pore structure, histol., and immunohistochem. Compared to previous studies, the authors found better penetration of cells into both types of scaffolds, with more extensive formation of new vessels throughout the construct but with only minor adipose tissue. The authors' encouraging results contribute towards a better seeded and vascularized scaffold but also show that the enhancement of adipogenic conversion of preadipocytes remains a major task for further in vivo expts.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 12 MEDLINE on STN
ACCESSION NUMBER: 2005400405 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15964623
TITLE: Implantation of preadipocyte-loaded hyaluronic acid-based scaffolds into nude mice to evaluate potential for soft tissue engineering.
AUTHOR: Hemmrich Karsten; von Heimburg Dennis; Rendchen Raoul; Di Bartolo Chiara; Milella Eva; Pallua Norbert
CORPORATE SOURCE: Department of Plastic Surgery and Hand Surgery, Burn Centre, University Hospital of the Aachen University of Technology, Germany.
SOURCE: Biomaterials, (2005 Dec) Vol. 26, No. 34, pp. 7025-37.
Journal code: 8100316. ISSN: 0142-9612.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200512
ENTRY DATE: Entered STN: 3 Aug 2005
Last Updated on STN: 15 Dec 2005
Entered Medline: 7 Dec 2005
AB The reconstruction of soft tissue defects following extensive deep burns or tumor resections remains an unresolved problem in plastic and reconstructive surgery since adequate implant materials are still not available. Preadipocytes, immature precursor cells found between mature

adipocytes in adipose tissue, are a potential material for soft tissue engineering since they can proliferate and differentiate into adipose tissue after transplantation. In previous studies, we identified hyaluronan benzyl ester (HYAFF 11) sponges to be promising carrier matrices. This study now evaluates, in vitro and in vivo, a new sponge architecture with pores of 400 microm either made of plain HYAFF 11 or HYAFF 11 coated with the extracellular matrix glycosaminoglycan hyaluronic acid. Human preadipocytes were isolated, seeded onto carriers and implanted into nude athymic mice. Explants harvested after 3, 8, and 12 weeks were examined for macroscopical appearance, thickness, weight, pore structure, histology, and immunohistochemistry. Compared to previous studies, we found better penetration of cells into both types of scaffolds, with more extensive formation of new vessels throughout the construct but with only minor adipose tissue. Our encouraging results contribute towards a better seeded and vascularised scaffold but also show that the enhancement of adipogenic conversion of preadipocytes remains a major task for further in vivo experiments.

L5 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:694981 CAPLUS
DOCUMENT NUMBER: 143:482971
TITLE: Implantation of preadipocyte-loaded hyaluronic acid-based scaffolds into nude mice to evaluate potential for soft tissue engineering
AUTHOR(S): Hemmrich, Karsten; von Heimburg, Dennis; Rendchen, Raoul; Di Bartolo, Chiara; Milella, Eva; Pallua, Norbert
CORPORATE SOURCE: Department of Plastic Surgery and Hand Surgery, University Hospital of the Aachen University of Technology, Aachen, D-52057, Germany
SOURCE: Biomaterials (2005), 26(34), 7025-7037
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The reconstruction of soft tissue defects following extensive deep burns or tumor resections remains an unresolved problem in plastic and reconstructive surgery since adequate implant materials are still not available. Preadipocytes, immature precursor cells found between mature adipocytes in adipose tissue, are a potential material for soft tissue engineering since they can proliferate and differentiate into adipose tissue after transplantation. In previous studies, the authors identified hyaluronan benzyl ester (HYAFF-11) sponges to be promising carrier matrixes. This study now evaluates, in vitro and in vivo, a new sponge architecture with pores of 400 μm either made of plain HYAFF-11 or HYAFF-11 coated with the extracellular matrix glycosaminoglycan hyaluronic acid. Human preadipocytes were isolated, seeded onto carriers and implanted into nude athymic mice. Explants harvested after 3, 8, and 12 wk were examined for macroscopical appearance, thickness, weight, pore structure, histol., and immunohistochem. Compared to previous studies, the authors found better penetration of cells into both types of scaffolds, with more extensive formation of new vessels throughout the construct but with only minor adipose tissue. The authors' encouraging results contribute towards a better seeded and vascularized scaffold but also show that the enhancement of adipogenic conversion of preadipocytes remains a major task for further in vivo expts.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 2 MEDLINE on STN
ACCESSION NUMBER: 2005400405 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15964623
TITLE: Implantation of preadipocyte-loaded hyaluronic acid-based scaffolds into nude mice to evaluate potential for soft tissue engineering.
AUTHOR: Hemmrich Karsten; von Heimburg Dennis; Rendchen Raoul; Di Bartolo Chiara; Milella Eva; Pallua Norbert
CORPORATE SOURCE: Department of Plastic Surgery and Hand Surgery, Burn Centre, University Hospital of the Aachen University of Technology, Germany.
SOURCE: Biomaterials, (2005 Dec) Vol. 26, No. 34, pp. 7025-37.
Journal code: 8100316. ISSN: 0142-9612.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200512
ENTRY DATE: Entered STN: 3 Aug 2005
Last Updated on STN: 15 Dec 2005
Entered Medline: 7 Dec 2005

AB The reconstruction of soft tissue defects following extensive deep burns or tumor resections remains an unresolved problem in plastic and reconstructive surgery since adequate implant materials are still not available. Preadipocytes, immature precursor cells found between mature adipocytes in adipose tissue, are a potential material for soft tissue engineering since they can proliferate and differentiate into adipose tissue after transplantation. In previous studies, we identified hyaluronan benzyl ester (HYAFF 11) sponges to be promising carrier matrices. This study now evaluates, in vitro and in vivo, a new sponge architecture with pores of 400 microm either made of plain HYAFF 11 or HYAFF 11 coated with the extracellular matrix glycosaminoglycan hyaluronic acid. Human preadipocytes were isolated, seeded onto carriers and implanted into nude athymic mice. Explants harvested after 3, 8, and 12 weeks were examined for macroscopical appearance, thickness, weight, pore structure, histology, and immunohistochemistry. Compared to previous studies, we found better penetration of cells into both types of scaffolds, with more extensive formation of new vessels throughout the construct but with only minor adipose tissue. Our encouraging results contribute towards a better seeded and vascularised scaffold but also show that the enhancement of adipogenic conversion of preadipocytes remains a major task for further in vivo experiments.

L7 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:889395 CAPLUS
DOCUMENT NUMBER: 137:375283
TITLE: Antiemetic, anti-motion sustained release drug delivery system
INVENTOR(S): Drizen, Alan; Nath, Gary M.
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 20 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002172712	A1	20021121	US 2001-810329	20010319
CA 2341998	AA	20020919	CA 2001-2341998	20010323
WO 2003009829	A2	20030206	WO 2002-US8013	20020318
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003175354	A1	20030918	US 2003-389959	20030318

PRIORITY APPLN. INFO.: US 2001-810329 A 20010319

AB This invention relates to a stable, sterilized, purified composition having a polymer matrix and a therapeutically effective amount of a drug, wherein the drug can be used to prevent or treat drug-induced, alc.-induced, biol.-induced, trauma-induced or pain-induced nausea, vomiting, dizziness and other adverse effects arising from but not limited to motion sickness, cancer therapy, and pregnancy. In particular, the polymer matrix may be conformable to topical application on animal skin. Polymer examples include hyaluronates and celluloses. A composition contained dimenhydrinate 1.5, Na hyaluronate 2.3, hydroxyethyl cellulose 0.7, methoxy-PEG 10, benzyl alc. 2.5% and water remainder.

L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:617437 CAPLUS
DOCUMENT NUMBER: 119:217437
TITLE: Drugs containing hyaluronic acid for the topical treatment of skin diseases.
INVENTOR(S): Falk, Rudolf Edgar; Asculai, Samuel Simon; Klein, Ehud Shmuel; Harper, David William; Hochman, David; Purschke, Don
PATENT ASSIGNEE(S): Norpharmco Inc., Can.
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 24
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9316732	A1	19930902	WO 1993-CA61	19930216
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK,				

UA, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG

CA 2061703	AA	19930821	CA 1992-2061703		19920220
CA 2061703	C	20020702			
AU 9334888	A1	19930913	AU 1993-34888		19930216
EP 626863	A1	19941207	EP 1993-903754		19930216
EP 626863	B1	20010425			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

JP 07506812	T2	19950727	JP 1993-514407		19930216
IN 175918	A1	19951028	IN 1993-CA94		19930216
HU 75089	A2	19970428	HU 1993-3282		19930216
PL 173211	B1	19980227	PL 1993-301149		19930216
NZ 299280	A	20001222	NZ 1993-299280		19930216
AT 200736	E	20010515	AT 1993-903754		19930216
ES 2156124	T3	20010616	ES 1993-903754		19930216
PT 626863	T	20010830	PT 1993-903754		19930216
CZ 290637	B6	20020911	CZ 1993-230		19930218
CN 1084064	A	19940323	CN 1993-103488		19930220
CN 1103219	B	20030319			
FI 9403789	A	19941003	FI 1994-3789		19940817
FI 113522	B1	20040514			
NO 9403044	A	19941019	NO 1994-3044		19940817
NO 312939	B1	20020722			
IN 179130	A1	19970830	IN 1995-CA272		19950313
IN 182267	A1	19990227	IN 1995-CA270		19950313
IN 182348	A1	19990327	IN 1995-CA271		19950313
IN 178280	A1	19970322	IN 1995-CA293		19950314
US 6140312	A	20001031	US 1995-466714		19950606
CA 2268476	AA	19980430	CA 1996-2268476		19961018
AU 9672721	A1	19980515	AU 1996-72721		19961018
AU 739701	B2	20011018			
EP 952855	A1	19991103	EP 1996-934250		19961018
EP 952855	B1	20050727			

R: DE, FR, GB, IT, SE

NZ 335259	A	20001222	NZ 1996-335259		19961018
ZA 9608847	A	19970527	ZA 1996-8847		19961022
US 6475795	B1	20021105	US 1997-860696		19970616
AU 9742732	A1	19980115	AU 1997-42732		19971020
HK 1005983	A1	20010817	HK 1998-105085		19980610
GR 3036164	T3	20011031	GR 2001-401015		20010702
US 2003036525	A1	20030220	US 2002-234355		20020904

PRIORITY APPLN. INFO.:

CA 1992-2061703	A	19920220
CA 1992-2061566	A	19920220
IN 1993-CA94	A1	19930216
WO 1993-CA61	A	19930216
WO 1996-CA700	A	19961018
US 1997-860696	A1	19970616

AB Compns. comprising hyaluronic acid and a nonsteroidal antiinflammatory agent or a neoplasm inhibitor are topical drugs for the treatment of skin diseases, especially cancers. A formulation comprised diclofenac sodium 45, Na hyaluronate 37.5, benzyl alc. 15, methoxypolyethylene glycol 300 g, and water to 1200 mL. The formulation was successful in the treatment of human basal cell carcinoma. Hyaluronic acid facilitates transport of the 2nd drug.

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     (FILE 'HOME' ENTERED AT 08:55:50 ON 11 DEC 2006)

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L21           0 S L19 AND CROSS LINK?
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     FILE 'CAPLUS, MEDLINE' ENTERED AT 17:44:07 ON 10 DEC 2006
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L2           25 S HYALURONIC ACID (P) ANGIOGEN? (P) TUMOR? (P) INHIBIT?
L3           38 S L1 NOT L2
L4            0 S L3 AND ESTER?
L5            0 S HYALURONIC ACID (P) ANGIOGEN? (P) TUMOR? SITE?
L6            0 S HYALURONATE ESTER? (P) ANGIOGEN? (P) TUMOR? SITE?
L7            0 S HYALURONATE (P) ESTER? (P) ANGIOGEN? (P) TUMOR? SITE?
L8            0 S HYALURONATE ESTER? (P) ANGIOGEN? (P) TUMOR?
L9           63 S HYALURONIC ACID (P) ANGIOGEN? (P) TUMOR?
L10          21 S HYALURONIC ACID (P) INHIBIT? (P) TUMOR? (P) SITE?
L11          19 S L10 NOT L2
L12          17 S HYALURONIC ACID (P) ESTER? (P) INHIBIT? (P) TUMOR?
L13           1 S HYALURON? (P) TUMOR? (P) ESTER? (P) INHIBIT? (P) ANGIOGEN?
L14           1 S ?HYALURON? (P) TUMOR? (P) ESTER? (P) INHIBIT? (P) ANGIOGEN?
L15           8 S ?HYALURON? (P) TUMOR? (P) DERIV? (P) INHIBIT? (P) ANGIOGEN?
L16          62 S ?HYALURON? (P) TUMOR? (P) INHIBIT? (P) ANGIOGEN?
L17          60 S L16 NOT L10
L18           9 S ?HYALURON? (P) TUMOR? (P) INHIBIT? ANGIOGEN?
L19          51 S L17 NOT L18
L20           1 S L19 AND CROSSLINK?
L21           0 S L19 AND CROSS LINK?
L22           0 S L19 AND CROSS-LINK?
L23           0 S L19 AND AUTOCROSSLINK?
L24           0 S ?HYALURON? (P) ?BENZYL? (P) TUMOR? (P) INHIBIT? (P) ANGIOGEN?
L25           0 S ?HYALURON? (P) ?BENZYL? (P) TUMOR? (P) INHIBIT?
L26           3 S ?HYALURON? (P) ?BENZYL? (P) CANCER? (P) INHIBIT?
L27          29 S ?HYALURON? (P) ?CROSS? (P) INHIBIT? (P) TUMOR?
L28           9 S ?HYALURON? (P) ?CROSSLINK? (P) INHIBIT? (P) TUMOR?
L29           0 S ?HYALURON? (P) ?CROSSLINK? (P) TUMOR? (P) SPONGE? (P) FILM?
L30          16 S ?HYALURON? (P) ?CROSSLINK? (P) SPONGE? (P) FILM?
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